

# **Protocol for the investigation of acute respiratory illness outbreaks of unknown etiology**

**Integrated Disease Surveillance Programme  
Health Security and Emergencies Cluster**



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## Acronyms and Abbreviations

AFRO	Regional Office for Africa
ARI	Acute respiratory illness
CBS	Community-Based Surveillance
CDC	United States Centers for Disease Control and Prevention
EBS	Event-Based Surveillance
FAO	Food and Agricultural Organization of the United Nations
GISN	Global Influenza Surveillance Network
GISRS	Global Influenza Surveillance and Response System
HA	Haemagglutinin
IFA	Immunofluorescence Antibody
HAI	Haemagglutination Inhibition
IBS	Indicator-Based Surveillance
IDSR	Integrated Disease Surveillance and Response
IHR	International Health Regulations (2005)
ILI	Influenza-like Illness
IPC	Infection prevention and control
LRTI	Lower respiratory tract infection
MERS	Middle East respiratory syndrome
MERS-CoV	Middle East respiratory syndrome coronavirus
MoH	Ministry of health
NA	Neuraminidase
NGO	Nongovernmental Organization
NIC	National influenza centre
NPS	Nasopharyngeal swab
OIE	World Organization for Animal Health
OPS	Oropharyngeal swab
PCR	Polymerase chain reaction
PHE	Public health event
PHEIC	Public Health Event of International Concern
RRT	Rapid Response Team
RSV	Respiratory syncytial virus
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
SARI	Severe Acute Respiratory Infection
SARS	Severe Acute Respiratory Syndrome
SARS-CoV	Severe Acute Respiratory Syndrome coronavirus
ToR	Terms of Reference
URTI	Upper respiratory tract infection
UTM	Universal Transport Medium
VTM	Viral Transport Medium
WHO CC	WHO collaborating centre
WHO	World Health Organization

# 1. Background

## 1.1 Global burden of respiratory disease

The burden of respiratory disease on global health is considered to be substantial, and the prevalence of upper respiratory tract infections (URTIs) was estimated at 18.8 billion cases in 2013 with an estimated 4 million deaths. Acute respiratory infections (ARIs), mainly pneumonia, are the leading cause of death for children under the age of five in developing countries, accounting for approximately three million deaths annually (1). URTIs are predominantly caused by viruses, and the sites of infection include mouth, nose, throat, larynx and trachea. In contrast, lower respiratory tract infections (LRTIs) can be caused by bacteria, viruses, fungi, mycoplasma or rickettsias and involve infection of the bronchial tubes and lungs, presenting as bronchitis, bronchiolitis or pneumonia. The bacterial agents responsible for transmissible ARIs in humans include *Mycobacterium tuberculosis*, which causes tuberculosis (TB), *Corynebacterium diphtheria*, which causes diphtheria, *Bordetella pertussis*, which causes whooping cough, *Yersinia pestis*, which causes pneumonic plague, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Streptococcus pyogenes*.

Although bacterial and viral diseases contribute to the global burden of respiratory disease, this document focuses on the detection of novel and emerging viral agents as causes of ARIs that may be responsible for outbreaks, epidemics or pandemics. Annex 1 provides a comprehensive, though not exhaustive, list of known agents that may cause ARIs.

A number of viruses cause mild respiratory diseases that are seldom fatal. These include adenoviruses, human metapneumovirus (hMPV), parainfluenza virus (PIV) types 1, 2 and 3, and rhinoviruses. Although respiratory syncytial viruses (RSVs) seldom cause serious disease in older children and adults, they often cause fatal infections in infants. Hantaviruses on the other hand can cause severe disease (Hantavirus associated pulmonary syndromes) but to date cases have been reported only in the Americas.

### **Coronaviruses**

Prior to the discovery of severe acute respiratory syndrome virus (SARS-CoV) and Middle East respiratory syndrome virus (MERS-CoV), the human coronaviruses HCoV-229E and HCoV-OC43 were known to cause mild respiratory diseases (causative agents in 15% – 30% of cases of the common cold), with the occurrence of severe disease being rare.

SARS was first recognized as an atypical pneumonia in China in late 2002, and by July 2003 the disease had spread to more than 29 countries on 4 continents, infecting 8098 people and resulting in 774 deaths (2).

The etiological agent causing SARS was established to be a novel coronavirus (SARS-CoV) initially transmitted from wild game (raccoon dogs and palm civet cats) to humans (3). Human-to-human transmission was responsible for the spread of the disease until it was contained in July 2003.

Soon after SARS-CoV was identified, two additional novel coronaviruses, HCoV-HKU1 and HCoV-NL63, which cause self-limiting upper respiratory tract infections, were identified. Although described as causing mild self-limiting infections, these viruses can cause more severe disease in the very young, the elderly and immunocompromised individuals (4, 5).

Middle East Respiratory Syndrome (MERS) was first identified as a serious respiratory disease resulting in high morbidity and mortality in the Middle East in 2012. Since then, over 1590 laboratory confirmed cases of the disease in humans have been reported to the World Health Organization (WHO), including over 570 associated deaths (6). Cases have been reported in over 25 countries, with the majority from the countries in the Middle East Region (83.2%), including the Kingdom of Saudi Arabia (1037 cases), United Arab Emirates (76 cases), Qatar (13 cases) and Jordan (12 cases) (7). Recently (May 2015), the disease was exported from the Middle East to the Republic of Korea by an infected traveller, which caused a significant healthcare associated outbreak with over 180 infections and over 30 deaths (8, 9). MERS, like SARS, is a zoonotic disease caused by the coronavirus MERS-CoV. Evidence-based data have linked transmission of MERS-CoV from camels or camel products (e.g. raw camel milk) to humans via either direct or indirect exposures; however, the exact mechanism of transmission is unknown (10). Human-to-human transmission of MERS-CoV has occurred in households and healthcare settings via droplets and direct contact with infected individuals; however, sustained human-to-human transmission in the community has not yet been reported (10).

To date, the spread of MERS has been somewhat geographically restricted in regard to its spread, with only one significant outbreak recognized outside of the Kingdom of Saudi Arabia. However, annual religious and cultural events in the region that attract millions of international visitors suggest that the virus could once again be exported, which may lead to the occurrence of multiple outbreaks in more countries.

### **Influenza**

Influenza is an acute viral disease in humans, often characterized by fever, headache, myalgia, prostration, coryza, sore throat and cough. Influenza infection is clinically indistinguishable from other viral associated respiratory illnesses without laboratory confirmation. Influenza viruses are classified as influenza types A, B and C. Only influenza A and B viruses can cause epidemic disease in humans while type C viruses usually cause a mild, cold-like illness.



Influenza A viruses can be subtyped according to their surface glycoproteins haemagglutinin (HA) and neuraminidase (NA). There are 18 HA and 11 NA subtypes (11). Many different combinations of HA and NA surface glycoproteins are therefore possible. Three HA subtypes (H1, H2 and H3) and two neuraminidase subtypes (N1 and N2) commonly cause human disease, however influenza virus infections caused by other HA and NA subtypes have been reported (11, 12).

Influenza viruses can undergo two types of mutational change: antigenic drift and shift. Antigenic drift results in small variations in the genetic make-up of HA and NA each year, prompting annual revision of influenza vaccine preparations to reflect the new genetic make-up of the virus. Antigenic shift is characterized by an abrupt or major change in antigenicity of the virus via reassortment of its HA and NA genes such that very few people in a population have immunity against this newly emerged virus. Antigenic shift sometimes results in the appearance of a novel influenza virus that can infect and be easily transmissible among humans, potentially leading to a pandemic. The circulation of novel influenza viruses causing disease poses challenges since these viruses may not be detectable by routine diagnostic procedures used for subtyping influenza viruses, due to mutational change.

### **Seasonal influenza**

Over the past two centuries, seasonal outbreaks of influenza disease in humans have occurred and were known to be caused by influenza; subtypes A(H1N1), A(H1N2), A(H2N2) and A(H3N2). Seasonal influenza is an acute infection that is easily transmitted from person to person, causing annual epidemics. Influenza epidemics usually occur during winter in temperate regions but influenza viruses may circulate throughout the year in tropical and subtropical climates with unpredictable seasonal peaks. Seasonal influenza epidemics can result in significant morbidity and mortality, particularly amongst the young (children under 5 years of age), the elderly (over 65 years of age), and the immunocompromised or those with co-morbidities such as asthma or other lung disorders, cardiovascular disorders, diabetes, neurological disorders or obesity.

### **Non-seasonal influenza: pandemic influenza**

Pandemic influenza occurs when there is efficient and sustained human to human transmission of a pathogenic influenza subtype to which few people are immune. In the last hundred years, four global pandemics have occurred: (i) the 1918 pandemic (influenza A(H1N1)) affected an estimated 500 million and killed 50–100 million people worldwide (13); (ii) the 1957 Asian flu pandemic (influenza A(H2N2)) which resulted in an estimated 2 million deaths globally with 1:4000 infected; (iii) the milder 1968 Hong Kong flu pandemic (influenza A(H3N2)) which resulted in an estimated 1 million deaths (14); and (iv) the more recent 2009 influenza A(H1N1)pdm09 pandemic. Unlike past influenza pandemics, international travel

facilitated the rapid geographic spread of the 2009 pandemic virus (A(H1N1)pdm09) to all six WHO regions in less than nine weeks where it caused significant morbidity and over 18 000 deaths (15).

Although the majority of cases during the 2009 pandemic were mild, resolving without antiviral treatment, mortality rates were highest among children, young adults and pregnant women with 90% of deaths occurring among those less than 65 years of age (16). Death in severe cases was caused by severe viral pneumonia. As with seasonal influenza, increased risk of death was associated with underlying medical conditions, including pregnancy, asthma or other lung disorders, cardiovascular disorders, diabetes, immunosuppression, neurological disorders and obesity (16). The number of laboratory confirmed deaths reported to WHO for the 2009 pandemic was 18 500, although this is thought to be a vast underestimate of the true global mortality. Significantly, 51% of estimated deaths occurred in Africa and South-East Asia (15).

### ***Non-seasonal influenza: avian influenza viruses in humans***

The first cases of human infection with avian influenza virus A(H5N1) were reported in Hong Kong Special Administrative Region in 1997. Since then, infections in wild birds or poultry have been reported in at least 62 countries, and 840 infections with 447 deaths have been recorded (cumulative number to October 2015) in 16 countries, representing 5 of the 6 WHO regions (17). Most patients with influenza A(H5N1) infection present with symptoms of fever, cough and shortness of breath and radiological evidence of pneumonia. The large majority of cases for which risk factor data are available indicate that direct contact with live or recently dead poultry is the most important risk factor for human A(H5N1) infection.

In addition to influenza A(H5N1), an increasing number of avian influenza A viruses (e.g. A(H7N9) and A(H7N7)) have been recognized as causing sporadic infections in humans. Human disease caused by some avian viruses can be mild; however, certain avian viruses can cause severe disease and death. In 2013, avian influenza A(H7N9) emerged as a human pathogen in China and to date laboratory confirmed cases and deaths have been reported from China, Hong Kong Special Administrative Region of the People's Republic of China and Taiwan (Taipei Centres for Disease Control) (18). Unlike other H7 viruses such as A(H7N7), which causes mild disease in humans, A(H7N9) causes severe disease characterized by rapidly progressing severe pneumonia. Although most cases reported contact with poultry, a definitive link between poultry and human infection has not been established (12).

Other avian influenza A viruses that cause disease in humans include: A(H6N1), A(H9N2) which circulates endemically in poultry in many regions of the world including Africa, and A(H10N8), which has caused sporadic cases of severe disease in humans.

The emergence of new pathogenic agents causing respiratory disease, e.g. SARS and MERS, and the continuous circulation and mutation of avian, porcine and human influenza viruses highlight the need for vigilance in the surveillance of respiratory disease at all levels of the health delivery system, and the necessity for rapid response to mitigate the expansion and spread of any respiratory disease outbreak caused by a novel pathogenic agent. Population movements as a result of travel, tourism, trade, religion, migration and conflict, coupled with the highly mobile nature of natural reservoirs of some viruses (e.g. influenza), facilitate the rapid global spread of novel respiratory pathogens. The contribution of zoonotic disease agents to the global disease burden is increasing. In a data set analysing human disease outbreaks in 219 countries spanning 1980 to 2013, 56% of the outbreaks were caused by zoonotic agents, highlighting the fact that most of the new human infections will likely originate from wildlife or livestock, making animal reservoirs important contributors to human disease outbreaks (19, 20).

## **1.2 Regional context of respiratory disease**

While seasonal influenza and other respiratory pathogens continue to impact morbidity and mortality in the African Region, new threats such as MERS-CoV and avian influenza A(H5N1) which have the ability to cause significant morbidity and mortality in the Region and throughout the world, have emerged.

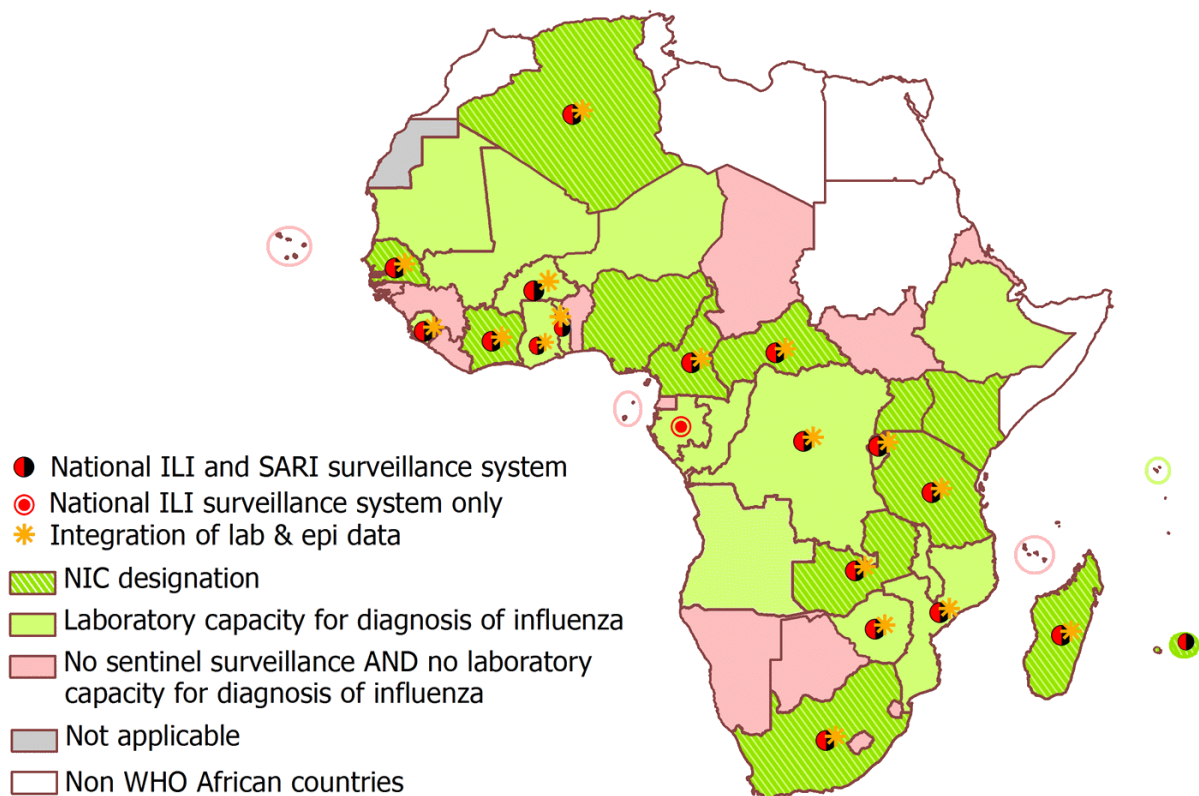
Although no cases of local transmission of SARS-CoV were reported in the African Region, (one imported case/death was reported in South Africa, [http://www.who.int/csr/sars/country/2003\\_05\\_03/en/](http://www.who.int/csr/sars/country/2003_05_03/en/)) and none have been reported globally since 2003, another coronavirus, MERS-CoV, emerged in 2012 in the Middle East. Since its emergence, MERS-CoV infections have been largely confined to the Middle East and to date over 75% of MERS-CoV cases have been reported in the Kingdom of Saudi Arabia. However, the accessibility of air travel and the increased number of global events such as the Hajj in the Kingdom of Saudi Arabia, human cases of MERS-CoV infection have been exported to a number of developed countries where cases have been quickly identified and the potential for a widespread outbreak mitigated, with the exception of the recent outbreak in the Republic of Korea. To date, only two human cases of MERS-CoV infection have been reported in the African Region. Both cases were identified in 2014 in travellers returning to Algeria from Umrah in the Kingdom of Saudi Arabia. As a result of intensive national preparedness activities, continuous human-to-human transmission did not occur in Algeria (21). Although no human cases have originated in countries in the African Region, serological evidence has indicated the presence of MERS-CoV circulating in camels in countries in the African Region (Ethiopia, Kenya and Nigeria) (22, 23).

Seasonal influenza viruses continue to be a major cause of morbidity and mortality in Africa. Sporadic cases of influenza can occur year round in tropical and subtropical regions, but the existence of seasonal patterns

of influenza transmission in the Region is not clearly defined and detailed data describing seasonality, epidemiology, transmission patterns and disease burden from human influenza in the African Region are limited. Current data suggest that influenza transmission patterns across this Region differ with geographical location, coinciding in some countries with lower environmental temperatures and rainy seasons and in others with cooler, dry periods (24). Nevertheless, influenza seasonality in most African countries remains unclear and difficult to assess (25).

Seasonal epidemics of severe influenza have occurred in the Region, in Madagascar and the Democratic Republic of the Congo in 2002, due to A(H3N2) and no country in the Region was spared from the global spread of pandemic influenza A(H1N1)pdm09 in 2009. Highly pathogenic avian influenza A(H5N1) continues to circulate in wild birds, causing disease in domestic poultry in the African Region. Since 2006, infections in poultry have been reported in nine countries in the African Region; however to date only a single human death has been reported (Nigeria in 2007) (26). In 2015, five countries in the region reported outbreaks of avian influenza A(H5N1) in either commercial flocks, backyard poultry flocks or live bird markets in some instances (27). The continued geographical spread of this highly pathogenic avian influenza virus among birds in Asia, Europe, the Middle East and Africa has heightened concerns about the possibility of a global human pandemic of influenza A(H5N1). Additionally, a new avian influenza virus, has emerged; influenza A(H7N9), causing human infections and deaths in China. Although this virus has not spread beyond China, aside from some exported cases, the possibility of this virus entering domestic bird populations in the Region is significant since a number of bird flyways traverse both Asia and Africa.

The implementation of influenza surveillance (ILI and SARI) has been a priority in the Region and the recent regional publication, *Protocol for national influenza sentinel surveillance*, aids Member States in establishing surveillance systems and contributing to regional influenza data. Laboratory capacity in the Region for the detection of influenza has also increased since the 2009 pandemic as part of the Pandemic Influenza Preparedness plan (PIP). Currently 30 of the 47 countries (64%) in the Region have the capacity to detect influenza by RT-PCR (Figure 1).



ILI = influenza-like illness, SARI = severe acute respiratory infection, NIC = national influenza centre

**Figure 1.** Distribution of influenza surveillance and laboratory activities in the African Region.

Source: *Integrated Disease Surveillance Quarterly Bulletin*, 2nd quarter data valid to 30 June 2015.(28)

Introduction of a new disease into a vulnerable population with weak or limited health systems and preparation and response capacity can have catastrophic effects as was evidenced with the Ebola virus disease outbreak in West Africa in 2014. This document aims to provide a protocol for Member States in the event of outbreaks of diseases caused by a pathogenic respiratory agent in line with the Integrated Disease Surveillance and Response (IDSR), the framework for the implementation of the International Health Regulations (IHR 2005) and the One Health approach.

### 1.3 IHR (2005) and IDSR

IHR (2005) requires Member States to meet core capacities with respect to surveillance, reporting, notification, verification, preparedness, response and collaboration activities for diseases that may constitute a public health event of international concern (PHEIC). To facilitate and simplify this decision-making process and to guide Member States, the IHR (2005) decision instrument was developed (Annex 7A). The IHR decision instrument enables diseases or disease events to be assessed in regard to their potential to cause a public health event with serious impact, if they are unusual or unexpected, if there is a risk of international spread, and if there is a risk that trade and travel restrictions may be implemented.

Importantly, the IHR decision instrument also defines disease caused by the following infectious agents: smallpox, poliomyelitis due to wild-type poliovirus, human influenza caused by a new subtype, and SARS, as events of international concern requiring immediate notification to WHO under the IHR regulations. Guidance on how to use the decision instrument including examples of its application in disease outbreak situations can be found at *WHO guidance for the use of Annex 2 of the International Health Regulations (2005), Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern (29)*. An example of the application of the IHR decision instrument for an infectious disease (cholera) is provided in Annex 7B.

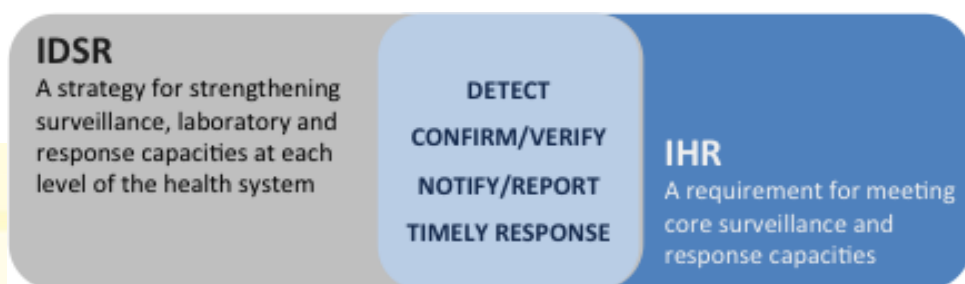
The IDSR strategy was first developed in 1998 with the core goal of strengthening the capacity of countries in the Region to conduct effective surveillance and response for multiple diseases by integrating and streamlining surveillance and response activities across all levels of the health sector (30). Following the 2009 influenza A(H1N1)pdm09 pandemic, the IDSR was reviewed and changes were implemented. The revised and expanded IDSR Technical Guidelines (2010) aligned with surveillance and response requirements outlined in IHR (2005) (31). Importantly, IDSR Technical guidelines (2010) incorporated diseases or PHEICs and a framework was developed for event-based surveillance and response.

The revised IDSR Technical Guidelines identifies a number of respiratory diseases as priority diseases; i.e. respiratory infections where;

- Identification is required under IHR (2005) (human influenza caused by a new subtype and SARS)
- They are diseases with a high epidemic potential (severe acute respiratory infection)
- They are the main causes of morbidity and mortality.

As per IHR (2005) requirements, Member States are required to build core capacities for surveillance, laboratory and response among others, as these diseases may result in a public event of international concern, for example an influenza pandemic.

IHR (2005) and IDSR share similar and complementary functions (Figure 2) and in the WHO African Region, activities recommended by the IHR are implemented in the context of IDSR.



**Figure 2.** Relationship between IDSR and IHR (30).



Considering the fact that a number of recent disease outbreaks affecting humans have originated in domestic animals (influenza A(H7N9) and influenza A(H5N1)), or wildlife (SARS and Ebola), the IDSR guidelines incorporate the One Health approach, promoting collaboration between national ministries of health and stakeholders in the animal health sector to identify and mitigate public health risks at the human–animal interface, such as sharing of surveillance information across wildlife, human and animal sectors and undertaking joint outbreak investigations.

#### **1.4 One Health approach**

One Health is defined as “the collaborative effort of multiple health science professions, together with their related disciplines and institutions – working locally, nationally, and globally – to attain optimal health for people, domestic animals, wildlife, plants, and our environment” (32).

It is recognized that a large proportion of the infectious diseases affecting humans that have emerged over the last 30 years have been zoonotic diseases, therefore, the contribution of animals and the environment to human health cannot be undervalued. Infectious agents continue to traverse the species barrier between animals and humans causing human disease. Notable examples of cross species transmission with subsequent explosive outbreaks of human diseases include SARS, influenza A(H1N1) and Ebola virus disease (EVD). Over the past decade, data has shown that 24% - 30% of all the major acute disease epidemics have had a zoonotic origin, with some of these diseases having pandemic potential. The current pandemic threats to the Region include viral haemorrhagic fevers (Ebola, Marburg, Lassa, Lujo, etc), Rift Valley Fever, influenza, plague and anthrax.

Urbanization, deforestation, land use and climate change are only a few of the factors that are influencing the interactions between the environment, animals and humans and thereby facilitating the emergence of new diseases, including those with epidemic and pandemic potential. The changing global environment, including the natural, physical, built and social environments, demands an interdisciplinary approach to health with collaboration between animal health, human health and environmental experts be adopted so that new disease threats can be recognized and abated in a timely fashion. The One Health approach, which was pioneered in the mid-2000s, addresses this gap, by bringing together expertise and organizations from all fields to address disease at the human–animal interface. For example, extensive work has been done aligning animal and human influenza surveillance activities, since controlling influenza at its animal source will not only protect animal health and maintain livelihoods, but will also prevent exposure of humans to animal pathogens and the possible emergence of a pandemic influenza strain. As such, the ‘Four-way Linking Project for Assessing Health Risks at the Human–Animal Interface’, a

collaboration between WHO, the World Organization for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO), was established in line with a tripartite agreement between these agencies (33). This project will capture epidemiological and virological data on animal and human influenza infections and link those data in time and space to provide a more informed, encompassing picture of influenza infection, and may aid in the rapid identification of locations where zoonotic infections may occur.

## 2. Scope and objectives

The occurrence of outbreaks of respiratory diseases, e.g. seasonal influenza, is not an unfamiliar global phenomenon. However, an outbreak of a novel influenza virus may have a catastrophic impact on local, national and global populations, including social and economic effects, if not identified in a timely fashion. Rapid identification of the causative agent of an outbreak enables rapid initiation of control and response activities and potential arrest of the outbreak before widespread national and global dispersal occurs. Preparedness facilitates rapid response to and control of outbreaks, lessening the impact of disease outbreaks, and forms the basis of this protocol.

### 2.1 Objectives

The objective of this protocol is to provide guidance for the investigation and control of an outbreak of respiratory disease with an unknown etiology in order to minimize morbidity and mortality associated with acute respiratory disease outbreaks.

This document aims to:

- (a) Provide Member States and stakeholders with technical guidance and methods employed to investigate and respond to ARI outbreaks;
- (b) Enhance multisectorial partnerships and communication so as to efficiently investigate and respond to outbreaks of ARIs of unknown etiology.

More specifically, this document provides a step-by-step guide to:

- (a) Enable Member States to investigate reports of sustained transmission of respiratory illness with epidemic potential caused by an unknown agent(s);
- (b) Evaluate cases of respiratory disease to characterize clinical characteristics, risk factor information, and epidemiological and microbiological features of an ARI outbreak of unknown etiology.



## 2.2 Target audience

The purpose of this protocol is to provide a comprehensive guide to those involved in public health responses to an outbreak of a respiratory disease of unknown etiology. While it is recognized that the IDSR Technical Guidelines provide a detailed framework for the investigation of diseases of known etiology, for those predominantly working in the healthcare arena, this protocol focuses on field investigations of respiratory diseases of unknown etiology from the human perspective. In this context, the target audience for this protocol includes, but is not limited to:

- (a) Senior decision/policy-makers;
- (b) Emergency response coordinators and managers;
- (c) Rapid response team (RRT) leaders;
- (d) Epidemiologists;
- (e) Laboratory scientists/technicians;
- (f) Clinicians/nurses/infection control experts/healthcare workers;
- (g) Data management experts;
- (h) Veterinarians/wildlife experts;
- (i) Social mobilization and communication experts.

## 2.3 Entities involved in outbreak investigation

An outbreak investigation transects all levels of the health system. It requires collaboration between the central coordination and administrative centres of the ministry of health and district/community health structures to facilitate effective preparedness, investigation and response activities for timely diagnosis and containment of an outbreak. The role of each entity will differ and is predominantly dictated by the type of infrastructure and expertise available. Typically, all levels of the health structure as well as other stakeholders such as livestock owners/farmers will be involved in an outbreak investigation (see Figure 3 and Annex 3). Briefly, entities involved in an outbreak investigation may include, but are not limited to:

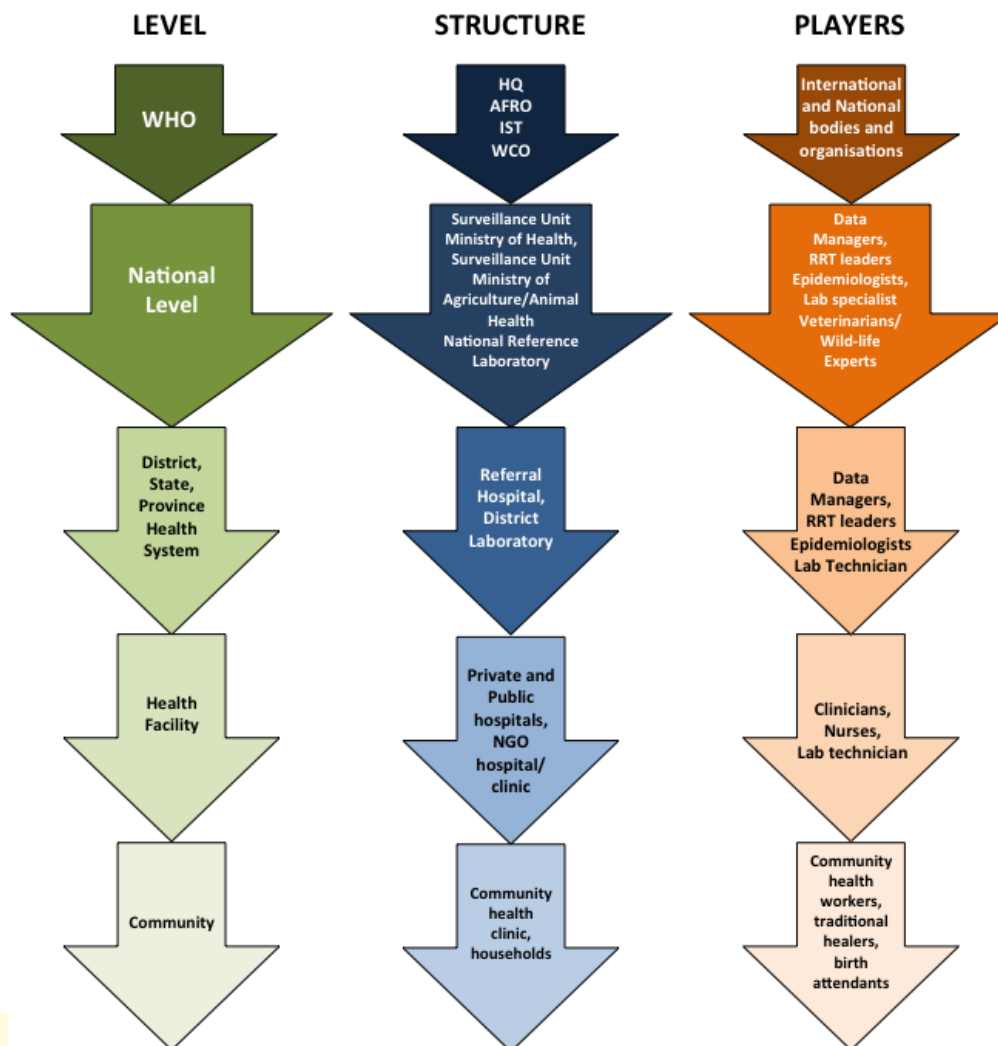
- (a) National level of health system/national level of agricultural and/or animal health system**
  - (i) Surveillance unit in the ministry of health;
  - (ii) Surveillance unit in the ministry agriculture;
  - (iii) National Reference Laboratories or National Influenza Centres.
- (b) District, state or provincial health systems**
  - (i) Intermediate administrative units;
  - (ii) Veterinary and animal husbandry officers;
  - (iii) Subnational, diagnostic laboratories, public, private and/or NGO facilities.
- (c) Health facilities with outpatient and/or inpatient facilities**
  - (i) Public hospitals/health clinics;

- (ii) Private hospitals/health clinics;
- (iii) NGO facilities.

**(d) Community level**

- (i) Community health centres;
- (ii) Traditional healers;
- (iii) Village health agents;
- (iv) Livestock owners and farmers.

Annex 3 provides a more detailed summary of entities that may be involved in an outbreak investigation, roles of entities and expertise generally available at that entity. Annex 3 is not an exhaustive list of all sites that may be involved in an outbreak or the roles a particular site may play in the outbreak or the type of expertise that may be available at each site mentioned.



**Figure 3.** Levels and structures in a health system and actors that may be involved in the investigation of a disease outbreak.

## 3. Detection of Respiratory Outbreaks

### 3.1 Definition of a disease outbreak

As defined by the World Health Organization, a disease outbreak is the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season or time period (34). Typically, outbreaks are not restricted by geography or time. An outbreak may extend across a number of countries or be limited to a small geographic area and can last anywhere between a few days to weeks, months or years, as evidenced by the 2014–2015 Ebola Virus Disease outbreak.

A single case of some diseases, for example, human influenza caused by a novel strain or the emergence of a previously unknown disease, may constitute an outbreak and require immediate notification and investigation in order to rapidly contain the event.

### 3.2 Respiratory disease outbreak indicators

The following list outlines some events and “triggers” that may indicate the possibility of a new or novel respiratory agent causing disease and that may be used as prompts to begin an investigation. The list is not exhaustive and has been categorized according to the site where initial identification of the outbreak may take place. These events may be detected during routine, event-based or community-based surveillance and may occur as suggested either in the community setting or at any level of the health system. As mentioned previously, this list is not exhaustive and any other unusual event(s), where individuals present with severe respiratory illness, should be investigated. If an event such as the one listed above is recognized at any level of the health system or in the community, reporting of the event to an appropriate authority or the next level in the health system is strongly recommended.

#### Identified at community level

- (i) Reports of multiple deaths or illness in fowl (poultry, ducks or other avian species) or other animals (swine, cats) occurring as a result of an outbreak;
- (ii) Acute respiratory illness in humans;
- (iii) Respiratory disease in humans who are in contact with sick animals;
- (iv) Reports of unusual events or occurrences at the local level, e.g. cluster of deaths, spike in the sale of particular pharmaceuticals, school or work absence;
- (v) Reports of rumours of deaths and/or of large numbers of sick people who are not presenting to health facilities;

- (vi) A cluster of respiratory illnesses or deaths for which the cause is not explained or is unusual;
- (vii) Radio, television or newspapers report(s) of a rumour of rare or unexplained events in an area with potential exposure for humans;
- (viii) Influenza/respiratory disease outbreaks outside the typical influenza season (when seasonality is well characterized);
- (ix) Clusters of influenza vaccine failures (if detected/reported);
- (x) Clusters of respiratory disease or pneumonia in families, schools, workplaces or community/family-based social networks;
- (xi) Change in the pattern of respiratory disease or pneumonia, i.e. an increase in mortality, shift in age group affected or change in clinical presentation;
- (xii) Changes in treatment responses (drug resistant organisms).

#### **Identified at the health facility/laboratory level**

- (i) Severe respiratory disease cases in healthcare workers;
- (ii) Respiratory disease in healthcare workers with a history of contact with patients with severe respiratory disease;
- (iii) Human cases of infection with an unsubtypable respiratory sample or any influenza virus not currently circulating in human populations;
- (iv) Unusually high levels of sales of pharmaceuticals used for respiratory illness;
- (v) An unusual increase in the number of cases or deaths during routine surveillance;
- (vi) Alert or epidemic thresholds have been reached;
- (vii) Routine review of records (higher levels of the health system) identifies an unusual number of cases of a particular disease/condition;
- (viii) Changes in the trend of respiratory disease observed in routine surveillance;
- (ix) Antiviral resistance.

### **3.3 Identification of an outbreak; Tools available for disease detection**

Disease surveillance is an important tool and may play a major role in the identification of an outbreak. In any Member State, disease surveillance may operate at a number of different levels, including:

- (i) Case-based syndromic surveillance (as indicated in IDSR);
- (ii) Sentinel surveillance, such as surveillance for influenza-like illness (ILI) and severe acute respiratory infection (SARI) (35);
- (iii) Community-based surveillance (CBS);
- (iv) Event-based surveillance (EBS).

In conjunction with IDSR implementation, Member States are encouraged to establish syndromic, case-based surveillance, which utilizes simple case definitions to identify cases and national sentinel influenza surveillance as part of the Pandemic Influenza Preparedness plan to enhance epidemiological and virological data on influenza in the African Region (35). Little is known regarding the epidemiological patterns, risk factors, burden of influenza disease and economic impact of influenza in the WHO African Region and data generated from the implementation of sentinel surveillance for influenza will address these knowledge gaps. More importantly, a robust sentinel influenza surveillance system (i) facilitates the detection and reporting of new strains of influenza viruses and may provide the first indication of a potential pandemic influenza virus or an agent causing respiratory disease for which there is no known etiology, (ii) provides timely notification of unusual cases or unusual numbers of cases of influenza, and (iii) provides a platform for the surveillance and identification of other epidemic- and pandemic-prone non-influenza respiratory pathogens (35).

Formal surveillance activities such as case-based syndromic and sentinel surveillance, in addition to other data sources (Table 1) are termed indicator-based surveillance (IBS). IBS transects many levels of the health system and predominantly involves healthcare professionals. In contrast, community-based surveillance (CBS) and event-based surveillance (EBS) rely on a variety of sources of information that are not organized or structured. Key players and sources of information in CBS and EBS include pharmacists, school teachers, private or nongovernment organization (NGO) clinics, village or religious leaders, traditional healers, birth attendants or other community health workers.

**Table 1.** Data sources that may contribute to surveillance of disease outbreaks

Sources of Information	
Indicator-based surveillance	Event-based surveillance
Mandatory notification of disease (case-based surveillance)	Media
Sentinel surveillance	Community
Syndromic surveillance	Internet, blogs, social networks
Mortality data	Informal networks
Laboratory data	Official websites
Routine registers eg. births/deaths	Alert networks
	NGOs
	Private sector
	Animal health
	Environmental disasters

Although IBS forms the cornerstone of disease detection, CBS and EBS are also useful tools for the detection of unusual disease activity.

In line with IDRS Technical Guidelines 2010, all levels of the health system are involved in conducting surveillance activities for detecting and responding to priority diseases and conditions. The development of event-based surveillance calls for community participation and the use of information technology products. The relevant IDSR data collection forms, designed for use at all levels of the health system, are now customized to capture PHEIC information (including diseases).

### ***Event-based surveillance (EBS)***

The cornerstone of an early warning and response system is the input of information from epidemic intelligence, which in turn relies on the collection of information and data from two complementary sources, namely IBS and EBS. While IBS data are collected via routine, sentinel, syndromic and disease-specific surveillance from conventional sources such as healthcare facilities, laboratories, death registers and other non-health sources using standardized methodologies and reporting mechanisms, EBS utilizes information and reports from any source. EBS data can be obtained from sources such as the media (local and national), the Internet (through social networks, blogs etc.), NGOs, informal networks, the private sector, veterinary services, points of entry and pharmacies. This information as the sources suggest, is not formally organized, is usually collected in real time and importantly its reliability is not assured. However, collection of EBS data effectively circumvents some of the complex processes associated with conventional surveillance systems, enabling implementation of a rapid response to a health threat, be it either perceived or real (36).

### ***Community-based surveillance (CBS)***

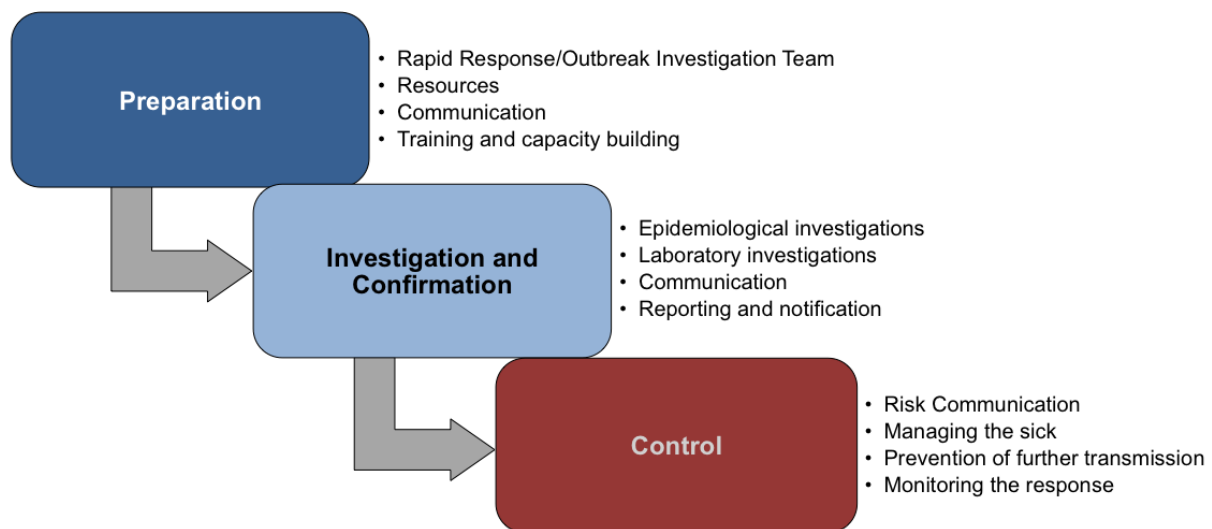
CBS represents a grassroots level for surveillance activities. It is a mechanism whereby, based on simple case definitions, priority diseases and unusual events or conditions, for example, unusually high mortality of animals or humans in a village, are recognized and reported in a timely manner by community representatives to a designated individual at a higher level in the health system to enable action, i.e. verification and investigation of the event.

Reported information on events is drawn from a variety of sources both within and outside the traditional healthcare setting, such as the local media, community-based organizations and families. CBS representatives ideally are drawn from those in routine roles in the wider community, including trained birth attendants, community or village health agents, care providers, village leaders (religious, traditional or political), school teachers, veterinarians, health extension workers, pharmacists and traditional healers. CBS can function to provide early warnings or alerts (pre-epidemic period), detect and respond to cases and deaths (the epidemic period) and monitor disease control activities (post-epidemic period) thus making it an integral component of national surveillance activities (36).

## 4. Steps in the Investigation of an Outbreak of Acute Respiratory Illness

Outbreak investigation goes hand in hand with outbreak response and control, both of which vary in importance depending on what is known about the causative organism. If both the mode of transmission and etiological agent causing the outbreak are known, the priority is on control of the disease outbreak. However, if both the mode of transmission and etiological agent are unknown or if there is suspicion that the disease's mode of transmission has changed, for example a zoonotic pathogen that now appears to spread efficiently between humans, investigation priorities focus on immediate measures to control the outbreak and investigation to define the pathogen and its transmission profile so as to better respond to and control the outbreak.

The steps in the field investigation of a disease outbreak are normally presented in a linear order. However, the reality of field investigations dictates flexibility with the focus on a systematic approach, speed and thoroughness. An investigation will usually proceed through three phases, namely preparation, investigation/confirmation and control (Figure 4).



**Figure 4.** Phases of an outbreak investigation

### 4.1 Preparation for the investigation

Preparedness for an outbreak aids in a timely response and rapid containment of the outbreak. To prepare for investigation of an outbreak the following actions should be initiated:

- Identify members of a rapid response team (RRT);
- Formulate the terms of reference (ToR) for the RRT or outbreak investigation team(s);
- Identify resources required for the field investigation (supplies, equipment and logistics);

- (d) Define communication plans for (i) communication with the public and (ii) communication with clinical/organizational stakeholders. The plan(s) should include how often and when to have conference calls and with whom and who will be the spokesperson. The plan should also include guidelines for the preparation of health alerts and press releases.

Other considerations for a field investigation are logistics, i.e. travel, lodging, local transport at outbreak location, shipping of clinical specimens to referral labs and coordination of meetings with local officials.

#### **4.1.1 Rapid Response Team (RRT)**

As a component of preparedness activities, a country should identify critical skills and individuals with those skills to form a RRT that can be easily and rapidly deployed to investigate a disease outbreak. The RRT is a multidisciplinary team of experienced experts from all areas of outbreak investigation and response. They should be available and on stand-by to respond to an outbreak in any region of a country within 24 hours. The role of the RRT is to assess the first case(s), provide healthcare (if appropriate), instigate investigations - epidemiological (case-finding, contact tracing etc.) and laboratory (collection and shipping of clinical specimens), provide recommendations on and initiate infection prevention and control (IPC) measures and engage with the community where necessary. The membership of a RRT depends on the outbreak circumstances, and may include:

- (i) Team leader
- (ii) Epidemiologist
- (iii) Clinician
- (iv) IPC expert
- (v) Veterinary and/or wildlife expert (if the disease agent is zoonotic and the disease also affects animals)
- (vi) Social mobilization expert
- (vii) Communication expert
- (viii) Logistician
- (ix) Laboratory expert

#### **4.1.2 Terms of reference (ToR)**

Terms of reference (ToR) should be established for the investigation team to provide a reference point for the specific aims, objectives and scope of the investigation. Terms of reference should define the role and purpose of the team, a time frame for the investigation/mission (if possible), membership of the team and the roles and responsibilities of each team members, and provide details or schedules of team meetings (if feasible) and reporting requirements of the team. Annex 4 outlines the potential roles and responsibilities of RRT members.



### **4.1.3 Resources required for outbreak investigation**

Identification of resources required for an outbreak investigation in the preparedness phase is critical for the safe and successful completion of an investigation and rapid control of an outbreak. Resources required by a RRT or first responders for a field investigation of a respiratory disease outbreak may include: personal protective equipment (PPE) (Annex 6A), specimen collection, packaging and shipping materials (Annex 6B), and outbreak investigation forms (Annex 6D). Other general items that may be required include: infection prevention and control supplies, risk communication materials, radio, GPS, maps, phones, camera, computer, chlorine, 5% sodium hypochlorite (bleach), buckets, sprayers, body bags, first aid kits and HIV post-exposure prophylaxis (PEP) kit. For a more comprehensive but not exhaustive checklist of general items that may be required for outbreak investigation refer to Annex 6C.

Depending on the RRT composition, the logistician should work with the team leader, laboratory expert, clinician/infection prevention and control expert as well as the epidemiologists in determining the supplies and any pre-positioning that is required. The RRT should be trained in use of the supplies provided, especially appropriate fitting of PPE and its safe disposal so as to protect each individual and prevent mechanical spread of the pathogen during the investigation process.

PPE is an essential component for RRT members and appropriate PPE in convenient sizes should be adopted if necessary when interviewing, examining, treating and collecting specimens from infected individuals or individuals suspected of being infected (see Annex 5 for guidance on the use of PPE). However, an emphasis should be placed on basic social distancing and hand hygiene practices. Sufficient stocks of PPE and supplies for maintaining hand hygiene should be obtained to provide protection for all individuals investigating the outbreak (37, 38).

At least one member of the RRT should be trained in the safe packaging and shipping of biological specimens.

### **4.1.4 Investigation team communication plan**

Prior to the departure of the RRT or outbreak investigation team a communication plan should be established. The plan should encompass communication within and between members of the RRT/outbreak investigation team. Components of a team communication plan may include:

- (a) Selection of an individual or agency as the outbreak coordinator. He/she/they will schedule and chair team meetings and review or receive copies of all communication.
- (b) Ensure that all sectors of the outbreak investigation team/RRT are represented at each meeting.
- (c) Scheduling of regular team meetings. Agenda items may include:
  - (i) Summary of outbreak, including any epidemiological and/or laboratory findings;
  - (ii) Update on progress of the investigation and identification of gaps to be addressed;

- (iii) Contributions from individual sectors;
  - (iv) Discussion of problems/barriers to outbreak investigation.
- (d) Determine a form(s) of communication (phone, fax, email, etc.) for team members outside the context of scheduled meetings as team members may be in diverse locations in the field.
  - (e) Developing a strategy/plan for release of health alerts and press releases if required.
  - (f) Preparation of a list of contact numbers for team members, ensuring that it is current and accurate.

Communication between the outbreak investigation team and health facilities, government departments, other agencies involved in the investigation, stakeholders and the public is discussed in a later section (Section 4.2.3).

#### **4.1.5 Training and capacity building**

As a component of the preparedness phase, training and capacity building focuses on training individuals in emergency preparedness and response. This may be achieved through scenario-based field training activities or simulation exercises. Participants in these training exercises ideally may include community, district and health facility personnel and individuals identified as members of RRTs. Review and analysis of the relevant literature, and other PHE response recommendations may also be useful in developing a capacity building programme. Additionally, existing WHO training materials may be used to complement or enhance training exercises or activities.

## **4.2 Investigation and confirmation**

### **4.2.1 Epidemiological investigations**

Collection and analysis of good quality epidemiological data is critical for an outbreak investigation as it informs response and containment activities. Data collected on carefully designed forms provide information on signs and symptoms, possible and known contacts and possible exposures or risk factors. The information gathered will be crucial to the development and refining of a case definition and will provide clues to the etiology of the outbreak and possible modes of transmission.

Epidemiological and laboratory forms required for an outbreak investigation may include, but are not limited to:

- (i) Case investigation form (Annex 6D.1)
- (ii) Patient line list (Annex 6D.2)
- (iii) Contact tracing form (Annex 6D.3)
- (iv) Contact follow-up form (Annex 6D.4)

Laboratory investigation forms

- (v) Line list of specimens tested and test results (Annex 6D.5)

If, during the process of an outbreak investigation, an animal link is identified, it is strongly recommended to engage experts from the veterinary and/or animal health fields to aid in the investigation.

### **Case definition**

For investigation of any outbreak, clearly defined case definitions are essential to select all cases or possible cases and to reduce time spent on patients with illness due to other diseases. A case definition is a set of criteria used for identifying individuals as having the disease of interest. During the course of an outbreak, a case definition may be further refined as information becomes available, to better reflect the disease and its etiology. Case definitions include critical clinical criteria based on objective measures and may be bound by time, place and person. However, a case definition is not limited to clinical findings and may also include other criteria such as animal contacts or hospitalization for example. One critical feature of a case definition is that it must be applied consistently to all patients under investigation. Annex 2 provides details on standard case definitions for priority respiratory diseases as per IDSR guidelines (2010) and other respiratory diseases of interest in an outbreak setting. In the absence of a case definition, common clinical symptoms can be used as a guide to identifying clinical infection.

In an outbreak, cases may be defined as (i) **suspected case**, (ii) **probable case** or (iii) **confirmed case**. In an outbreak where the etiology is unknown, the case definition should be sensitive enough to identify all possible, suspected and probable cases. The case definition can be further refined as the investigation progresses to reflect new clinical findings from cases investigated. When the etiological agent causing an outbreak is known, a more specific case definition that incorporates laboratory confirmation may be more desirable.

### **Case finding**

Case finding is an active process whereby suspected and probable cases as defined by the established case definition are sought from the population at risk, through contact tracing (described below), active case-finding and enhanced surveillance. In active case-finding and enhanced surveillance emphasis should be placed on:

- (i) Persons who may have been co-exposed to the same source as the case patient,
- (ii) Persons with similar environmental or occupational exposures;
- (iii) Persons with unexplained acute lower respiratory infection with fever and/or persons who died of an unexplained respiratory illness with fever.

Case-finding may involve reviewing health facility records, including hospitals, laboratories, private health clinics, and community visits such as to schools or house-to-house searches. Communication with community leaders should be initiated prior to case-finding activities in a community. Public

announcements may be used to identify remaining and/or unreported cases. Regardless of the method, systematic approaches to active case-finding and enhanced surveillance during the investigation should be established and the established case definition should be applied.

Once data have been collected, cases are usually stratified as suspected, probable or confirmed but may also be classified as laboratory confirmed and epidemiologically linked and defined as follows:

- (e) Suspected case: an individual where signs and symptoms meet the case definition;
- (f) Probable case: any suspected case with an epidemiological link to a confirmed case or animal exposure, but without laboratory confirmation;
- (g) Confirmed case: a suspected case where diagnostic laboratory results have confirmed the infection.

In addition to case finding and contact tracing activities in locations where cases reside, consider enhancing existing surveillance systems in these locations, where animal outbreaks are occurring or where the source of infection is suspected. The aim being to detect cases that might arise subsequent to the discovery of the initial cases. The geographical area targeted will depend on the outbreak context, in particular the suspected exposures for the outbreak.

The duration of enhanced surveillance will depend on the findings of the investigation, the pathogen causing the outbreak and whether there is evidence indicating that sustained transmission may be occurring in the area. For example, for outbreaks of avian influenza A(H5N1) infection, surveillance should be enhanced for two weeks after the last human case and for MERS-CoV one month after the last case.

The scope of the enhanced surveillance activities depends on the healthcare seeking behaviour of the population; it can include a range of options such as active and passive approaches that are health facility- and community based. Enhanced surveillance activities are generally conducted in hospitals but should also include other healthcare service settings such as private practitioners, laboratories and traditional healers. Lastly, consider also including groups at higher occupational risk of exposure such as healthcare workers and persons exposed to live or dead animals. Build enhanced surveillance on systems that are already in place using supplementary measures such as telephone hotlines, rumour tracking and verification, and radio or other emergency networks as needed for reporting suspected cases in the community.

The success of enhanced surveillance efforts will depend on training of health professionals, local public health investigators and volunteers, and education of the community-at-large to be alert for possible cases. In particular, encourage early self-reporting of illness and consultation with public health facilities such as establishing fever clinics so that prompt and appropriate testing and clinical care can be provided. In

addition, provide the affected community with appropriate education and prevention and intervention measures to reduce the risk of acquiring infection from human and animal sources.

### **Data collection**

The collection of clinical, laboratory and epidemiological data from cases is the cornerstone of an epidemiological investigation and the collection of comprehensive, good quality data from identified cases is critical. The case investigation form(s) should therefore be designed so as to collect all relevant information from the investigation. At the minimum, a case investigation form(s) should collect the following information from patients; identifying information (name, address/location, telephone number); demographic information (age, sex, ethnicity, occupation etc.); clinical information (clinical symptoms, date of onset of symptoms etc.); possible risk factors (exposures such as association with animals, food consumed and travel history); and information about attempted treatment. A template for a case investigation form is provided in Annex 6D.1. This data may then be used to compile a line list of affected individuals (see Annex 6D.2). The line list summarizes the patient data and should include information such as age, sex, symptoms onset date, duration of symptoms, location, case category, any epidemiological links, specimens collected and laboratory results, if known. Other information may be included in the line list as deemed necessary, as the line list is not limited to information collected from the case investigation form or features mentioned above.

### **Contact tracing**

The main aims of contact tracing is to identify, in a timely manner, new cases to limit the spread of an outbreak, and to understand the transmission dynamics of the causative agent by early detection, isolation and clinical management of new cases. In an epidemiological investigation, contact tracing has three elements, namely (i) contact identification; (ii) contact listing; and (iii) contact follow-up which usually occurs over a specified time period (normally a minimum of one incubation period, if that is known for the disease). Contact tracing activities should include all suspected, probable and confirmed cases as well as suspected deaths resulting from infection with the pathogen. Death due to the suspected pathogen may be verified by a verbal autopsy. Contacts can be classified as:

- (i) Close contact: an individual(s) who had had direct contact, defined as being within a distance of less than 1 m from a case and/or had discussion of more than three words with a case.
- (ii) possible or casual contact

A close contact may have had face-to-face contact with the patient, shared a meal or the same room with the patient, cared for the patient during the infectious period or contacted the patient's belongings. A possible or casual contact may have been exposed to the patient through other circumstances. An example of a contact listing form is provided in Annex 6D.3. A separate contact listing form should be completed for each case under investigation. Contacts should be followed for a defined period of time i.e. a time period greater than the incubation period for the disease being investigated, and data recorded indicating if they (the contact) are exhibiting signs or symptoms. If a contact shows signs and symptoms for the disease

under investigation, appropriate measures should be taken to isolate and treat the individual. This individual then becomes a suspected or probable case and subsequently his/her contacts would likely be followed-up.

### **Data analysis**

Once data has been collected it can be summarized (line list) and analysed so as to provide a description of the outbreak with relation to person, place and time. An in-depth epidemiological analysis may also be conducted to further characterize and understand the outbreak, including risk factors. The analysis may also then guide a revision of the case definition to more accurately identify cases, facilitate understanding of the mode and source of disease transmission and guide response strategies such as control, communication and prevention activities. Data outputs from the analysis may include, but are not limited to:

#### **Time**

- **Epidemic curve** (epi curve). An epi curve details the number of cases over time in an outbreak. From an epi curve one can observe the distribution of cases over time, identify outliers, determine the magnitude of the outbreak, the speed and possibly the mode of spread, and determine the time period of exposure or the incubation period for a disease with unknown etiology (39).

#### **Place**

- **Spot map** - is a visual interpretation of the data that provides details on the geographical extent of the outbreak. Data on residence or presumed site of exposure of cases is used for this analysis. A spot map can be used to identify outbreak clusters or patterns and may provide clues to the source of the etiological agent. The map may be local, regional or national, depending on the geographical spread of the outbreak. Collecting information on cases using GPS can be informative in identifying zone(s) of high transmission or spread of the disease.
- **Area map** - considers the number of cases in relation to the population in an area. This allows for direct comparison of incidence rates between regions, villages, states, provinces etc.

#### **Person**

- This analysis focuses on personal characteristics of cases such as age, sex, occupation, co-morbidities and exposure history. These items are examined to determine common features that may be useful in identifying new cases and those most at risk of infection. From these data it should be possible to determine a case fatality rate.

Together, these outputs characterize the outbreak to provide insights on the etiology, source and mode of transmission of the pathogen and define at-risk populations.

After the descriptive epidemiological analyses have been conducted and possible source(s) of infection and mode(s) of transmission identified, further studies such as case-control studies or serosurveys should be considered to better elucidate these transmission risks. The MERS-CoV case-control study protocol can serve as a model and can be modified for an outbreak of respiratory disease of unknown etiology (40, 41). Serosurveys can also be used to sharpen the case count, estimate asymptomatic infection attack rates and identify those truly at risk of developing illness. Such studies can also be used to improve the sensitivity/specificity of the case definition or determine degrees of exposure and dose response. Taken together, the epidemiological, laboratory and clinical data will provide compelling evidence and enable inferences to be drawn on the cause, source and transmission patterns of the disease.

#### **4.2.2 Laboratory investigation**

To identify the causative agent of an outbreak, a laboratory investigation must be initiated. The investigation will involve the safe collection of adequate clinical specimens from infected individuals, the proper storage and shipment of these specimens to a designated laboratory and the use of appropriate diagnostic technologies to determine the responsible pathogen. Prior to deployment to the field, agreement should be confirmed with an appropriate laboratory for testing, either an “in country” laboratory, if laboratory capacity is available, or an international reference laboratory if national capacity is limited or if further characterization is required. Agreement should also be reached with an appropriate courier/transportation service for transportation of specimens to the designated laboratory.<sup>1</sup>

When the causative pathogen is unknown, it is preferable to collect as many clinical specimens as possible from an infected individual. Investigators should be guided by clinical findings and available knowledge on diagnostic specimen selection for known pathogens when deciding on the most appropriate specimen to collect in an outbreak of unknown etiology. At the minimum, in the case of a respiratory infection, one specimen from the upper and lower respiratory tract should be collected. Collection of other clinical specimens such as blood, urine and faeces is advantageous and should be attempted.

Based on the suggested etiology of the disease, appropriate specimens should be collected from suspected cases for laboratory testing so as to identify the responsible pathogen as rapidly as possible. Logistical arrangements for the transportation of specimens to an appropriate laboratory for pathogen identification should be finalized during the preparation phase for the investigation. As soon as the specimens are

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<sup>1</sup> WHO Shipping Fund Project provides shipping services for national influenza centres to share influenza specimens. For detailed information please contact WHO headquarters: [gisrs-whohq@who.int](mailto:gisrs-whohq@who.int).



collected and shipped, the identified laboratory should be informed regarding the number, type of specimens, key epidemiological information, courier information and expected arrival time so as to be ready to receive and process specimens (Figure 5) as soon as they arrive in the laboratory. Although some diagnostic technologies do not require a live pathogen, appropriate collection, storage and transportation of patient specimens are critical to maintain viability of an organism for detection. Checklists for laboratory supplies and other items required for a RRT or for collection of specimens in the field are found in Annex 6B.

### **Specimen collection**

The following tables indicate the types of specimens that may be collected for respiratory infections. Table 2 indicates the types of specimens that may be collected from a patient/case and the recommended shipping and storage requirements, while Table 3 outlines the types of specimens that may be collected for laboratory diagnosis if a specific agent is suspected of causing disease. If a viral infection is suspected it is recommended that clinical specimens are collected in viral transport medium (VTM) or universal transport medium (UTM).

Aliquoting of specimens is recommended **only** if this can be performed in a safe (suitable, certified biosafety hoods(s) are available (42)) and sterile manner during sample collection or processing in field conditions. Appropriate PPE (see Annex 5) should be used when collecting and aliquoting specimens and all material used in specimen collection and aliquoting should be disposed of appropriately. Guidelines for the collection of specimens from patients, including children and deceased patients can be found in *Collecting, preserving and shipping specimens for the diagnosis of avian influenza A(H5N1) virus infection: guide for field operations* (43).



**Table 2.** Type of specimens for laboratory testing to detect the presence of respiratory disease pathogens and their handling

Type	Transport medium	Transport to laboratory <sup>#</sup>	Storage till testing	Comment
<b>Lower respiratory tract</b>				
Sputum	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	There is need to ensure that the material is from the lower respiratory tract
Bronchoalveolar lavage	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	There may be some dilution of the pathogen but collection of this specimen is still worthwhile.
Tracheal aspirate	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	
Endotracheal aspirate (patients on mechanical ventilation)	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	
<b>Upper respiratory tract</b>				
Nasopharyngeal aspirate	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	
Nasal wash	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	
Nose/throat swab	VTM	4 °C	≤ 5 days: 4 °C > 5 days: -80 °C	If a VTM is not available, swabs may be stored in ethanol; however, such specimens will be suitable only for PCR analysis
Nasopharyngeal swab	VTM	4 °C	≤ 5 days: 4 °C > 5 days: -80 °C	
<b>From deceased individuals</b>				
Biopsy or autopsy tissue, including from the lungs	VTM or saline	4 °C	≤ 24 hours: 4 °C > 24 hours: -80 °C	
<b>Other</b>				
Serum	NA	4 °C	≤ 5 days: 4 °C > 5 days: -80 °C	Collect paired samples. Acute – first week of illness. Convalescent – 2 to 3 weeks later
Whole blood	EDTA* tube	4 °C	≤ 5 days: 4 °C > 5 days: -80 °C	For antigen detection, particularly in the first week of illness
Urine	NA	4 °C	≤ 5 days: 4 °C > 5 days: -80 °C	
Faeces	NA	4 °C	≤ 48 hours: 4 °C > 48 hours: -80 °C	Collect 1–3 specimens of solid material (5 g = pea size) or 5 ml of liquid in a screw cap vial

\*The patient will undergo an aerosol generating procedure.

VTM = viral transport medium

NA = not applicable

**Table 3.** Clinical specimens collected for specific agents causing respiratory disease

Infectious agent	Specimens					
	Nasopharyngeal swab (NPS)	Oropharyngeal/throat swab (OPS)	Sputum	Blood/serum	Blood (culture)	Urine
Influenza A or B	✓	✓		✓		
Respiratory syncytial virus	✓ or nasal wash/aspirate			✓		
Human metapneumovirus <sup>a</sup>	✓					
Adenovirus			✓			
Parainfluenza virus (types 1, 2 and 3) <sup>b</sup>	✓			✓		
Human coronaviruses (hCoV-229E, hCoV-OC43, hCoV-HKU1, hCoV-NL63)	✓	✓				
SARS-CoV	✓			✓		
MERS-CoV <sup>c</sup>	✓	✓	✓	✓		
Hantaviruses <sup>d</sup>				✓		
<b>Bacteria</b>						
Diphtheria ( <i>Corynebacterium diphtheriae</i> )	✓					
Pertussis ( <i>Bordetella pertussis</i> )	✓					
Pneumonic plague ( <i>Yersinia pestis</i> )			✓	✓	✓	
Scarlet fever ( <i>Streptococcus pyogenes</i> )		✓		✓		
<i>Streptococcus pneumoniae</i> <sup>f</sup>			✓		✓	✓
<i>Haemophilus influenzae</i>			✓	✓	✓	
<i>Mycoplasma tuberculosis</i>			✓			
<i>Mycoplasma pneumoniae</i>			✓	✓	✓	

<sup>a</sup> Respiratory secretions from the nose or throat or nasal aspirate

<sup>b</sup> Respiratory secretions

<sup>c</sup> Additional specimens that may be collected include, bronchioalveolar lavage, tracheal aspirate or pleural fluid

<sup>d</sup> Can also be detected in tissue samples using immune histochemistry

<sup>e</sup> Respiratory secretions, lung tissue or pleural fluid

<sup>f</sup> Pleural fluid and lung aspirates are also suitable samples

NPS = nasopharyngeal swab

OPS = oropharyngeal swab

### **Specimen packaging and shipping**

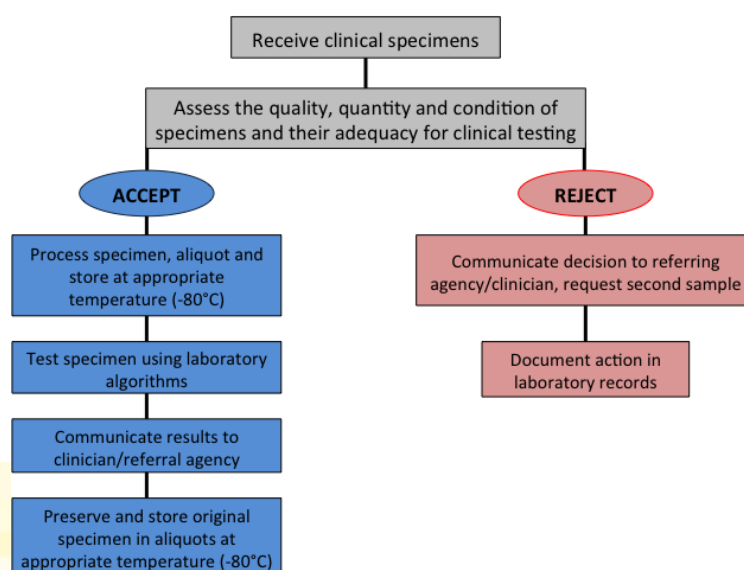
For the detection of pathogens by PCR, isolation or antibody testing inadequate or inappropriate specimen storage and transport can result in false negative results. When specimens are ready to be packed for transportation from the field or sentinel site to the laboratory, it is necessary to follow directions provided in *Guidance on Regulations for the Transport of Infectious Substances, 2015–2016*. [http://www.who.int/ihr/publications/who\\_hse\\_ihr\\_2015.2/en/](http://www.who.int/ihr/publications/who_hse_ihr_2015.2/en/). A brief guide of the packaging required for the safe shipment of clinical specimens is provided below:

- The **primary container**, which contains the specimen, must be leak-proof and watertight. Examples of primary containers include: Vacutainer with adhesive tape around cap, conical screw-cap tubes with parafilm around the cap or cryovials. Do not use Eppendorf tubes with tape or parafilm around the cap.

- The **secondary container** may contain several primary containers. The secondary container must also be leak-proof and watertight. Examples of watertight secondary containers include Ziploc plastic bags, conical 50ml test tubes and screw-cap containers.
- **Absorbent material** must be placed between the primary and secondary containers. The quantity should be sufficient to absorb all liquid in the shipment. Examples of suitable absorbent material include paper towels, cotton balls, filter paper, etc.
- If dry ice is needed to keep specimens frozen, it should be put between the secondary and tertiary/outer containers. Styrofoam and cardboard both allow dry ice vapour to escape, so dry ice must be placed **outside** the secondary packaging, never within the secondary container. Packaging dry ice inside impermeable, screw-cap secondary containers may cause the container to explode. Additionally, specimens should be in an airtight container as carbon dioxide from dry ice can inactivate the virus.
- The **tertiary or outer shipping container** must protect the inside packaging to avoid breakage or perforation under normal transport conditions. Corrugated cardboard is the usual choice. Styrofoam boxes, plastic bags or paper envelopes are unacceptable as outer containers for shipping biological materials.

It is important to keep specimens cold during transportation. Try to store specimens at 4 °C. A cooler filled with ice packs can be used for this purpose.

Be sure to coordinate shipment with the receiving laboratory. An itemized list of specimens (case investigation form) with specimen identification numbers and instructions for the laboratory must be included with all specimen shipments.

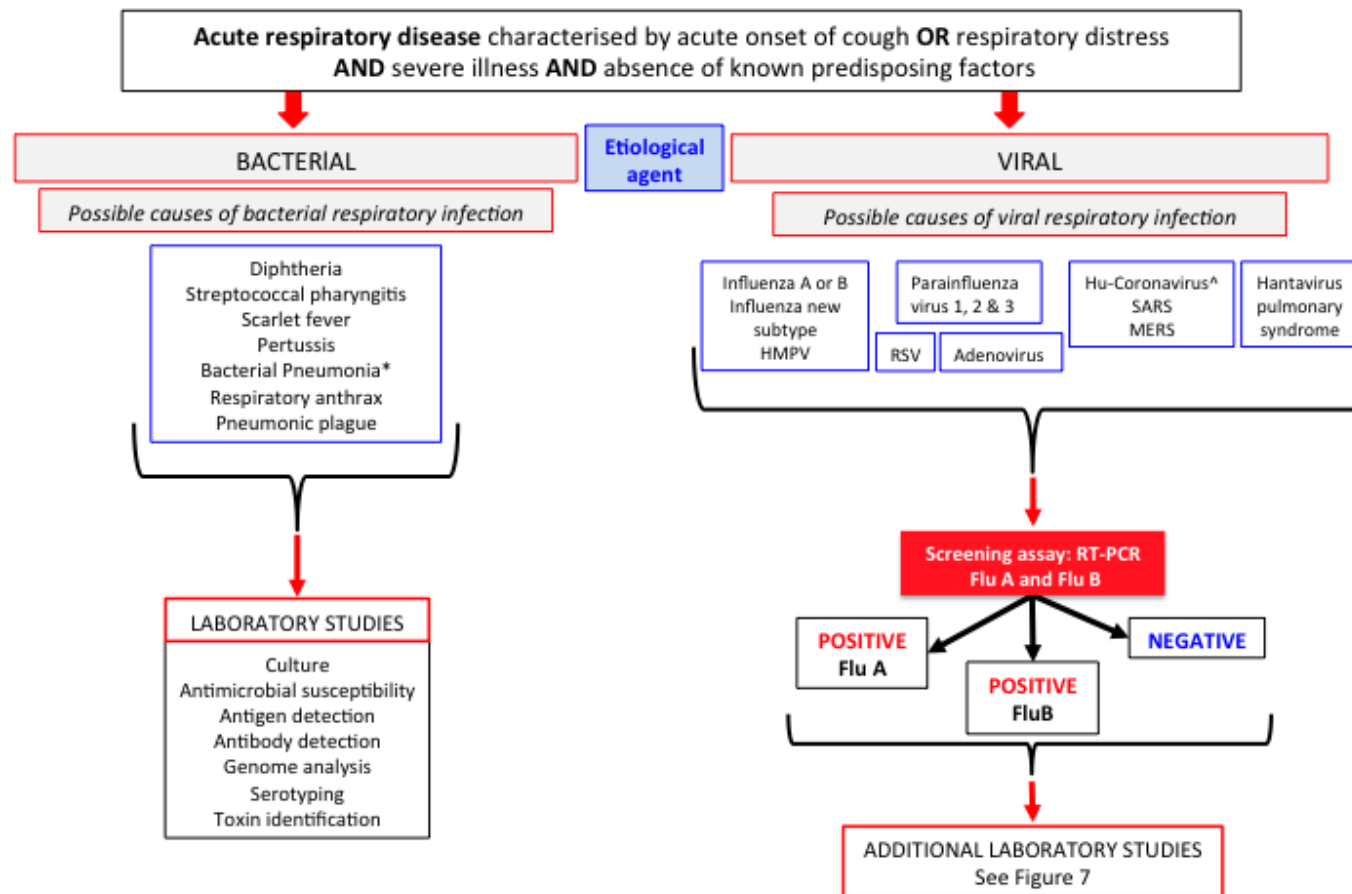


**Figure 5.** Flow of clinical specimens in the laboratory.

Source: Adapted from (44)

**Laboratory algorithm**

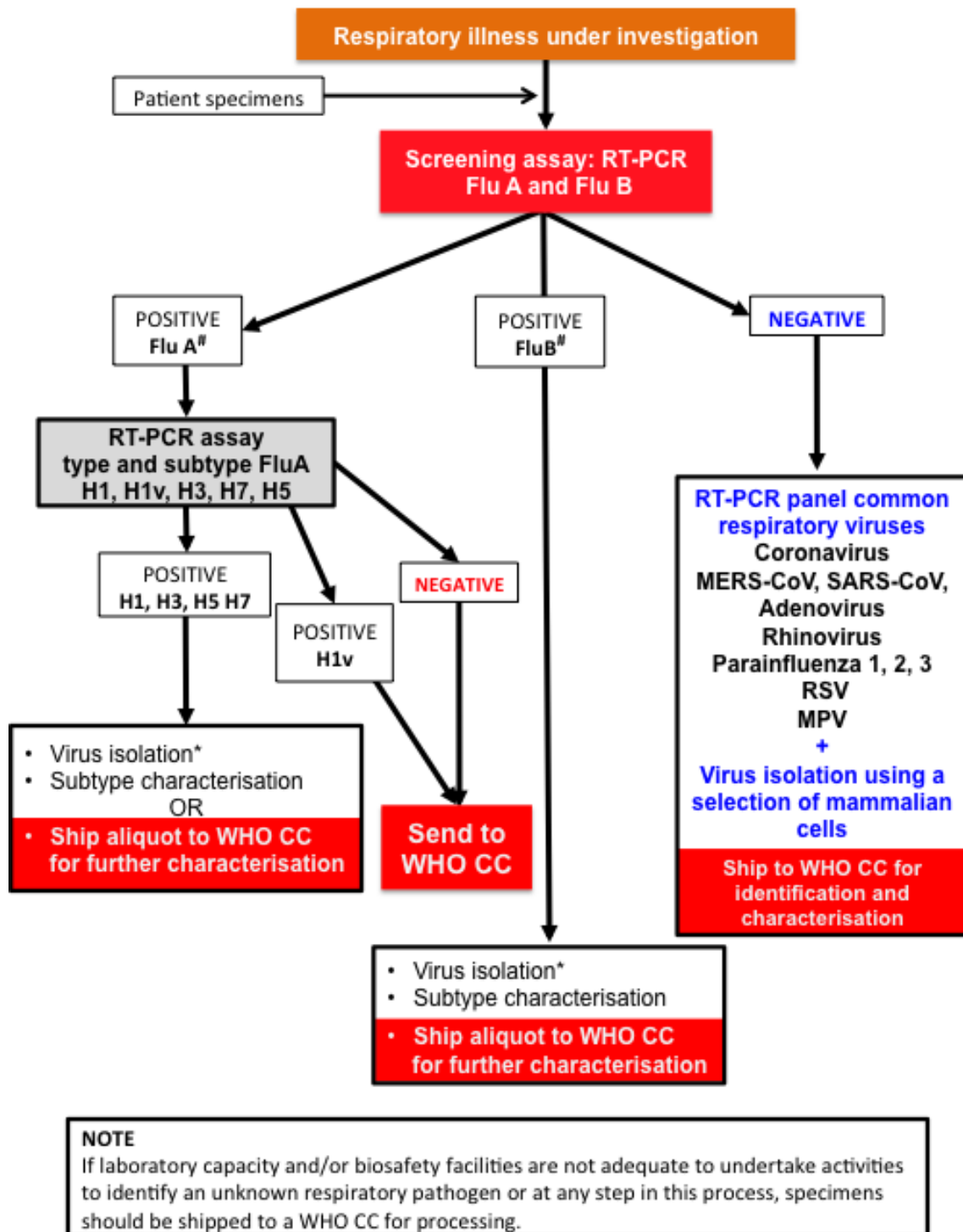
If a viral agent is suspected, the following algorithms, depicted in figures 6 and 7 can be followed to investigate the etiology of the causative agent. Table 4 provides a list of suggested diagnostic laboratory tests if the etiology of the pathogen is known.



\*Bacterial pneumonia includes pneumonia caused by *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Legionella* sp., Pneumococcal pneumonia  
<sup>^</sup> Human coronaviruses (hCoV-229E, hCoV-OC43, hCoV-HKU1, hCoV-NL63)

**Figure 6.** Laboratory algorithm, Part I

Source: Adapted from (45)



**Figure 7.** Laboratory algorithm Part II (if a viral agent is suspected, i.e. bacterial origin is excluded).

**Table 4.** Laboratory tests commonly used for the diagnosis of respiratory pathogens

Infectious agent	Diagnostic assay					
	Virus isolation <sup>#</sup>	IFA	HIA	PCR	Bacterial culture	Serology
Virus						
Influenza A or B*	✓	✓	✓	✓		
Respiratory syncytial virus	✓			✓		
Human metapneumovirus <sup>a</sup>	✓	✓		✓		
Adenovirus				✓		
Parainfluenza virus (types 1, 2 and 3) <sup>b</sup>	✓					
Human coronaviruses (hCoV-229E, hCoV-OC43, hCoV-HKU1, hCoV-NL63)				✓		
SARS-CoV	✓			✓		
MERS-CoV <sup>c</sup>				✓		
Hantaviruses <sup>d</sup>						✓
<b>Bacteria</b>						
Diphtheria ( <i>Corynebacterium diphtheriae</i> )					✓	
Pertussis ( <i>Bordetella pertussis</i> )				✓	✓	✓
Pneumonic plague ( <i>Yersinia pestis</i> )					✓	✓
Scarlet fever ( <i>Streptococcus pyogenes</i> )					✓	
<i>Streptococcus pneumoniae</i> <sup>g</sup>					✓	
<i>Haemophilus influenzae</i>					✓	
<i>Mycoplasma tuberculosis</i>				✓	✓	
<i>Mycoplasma pneumoniae</i>				✓		

\* Rapid influenza detection tests (RIDT) can be used for diagnosis of influenza A and B however they have limited sensitivity and specificity

<sup>#</sup> cell culture or eggs

IFA = immunofluorescence antibody

HAI = haemagglutination inhibition assay

PCR = polymerase chain reaction

#### 4.2.3 Information flow and communication

A communication plan encompassing all facets of the outbreak should be developed early and should include strategies for communication with the public, government agencies, health facilities and clinical/organizational stakeholders. This document does not aim to provide a definitive communication guide but focuses on communication necessities for the RRT/outbreak investigation team and for players at the district level, i.e. communication within the team, communication with relevant levels of the health system and agencies and communication with the public.

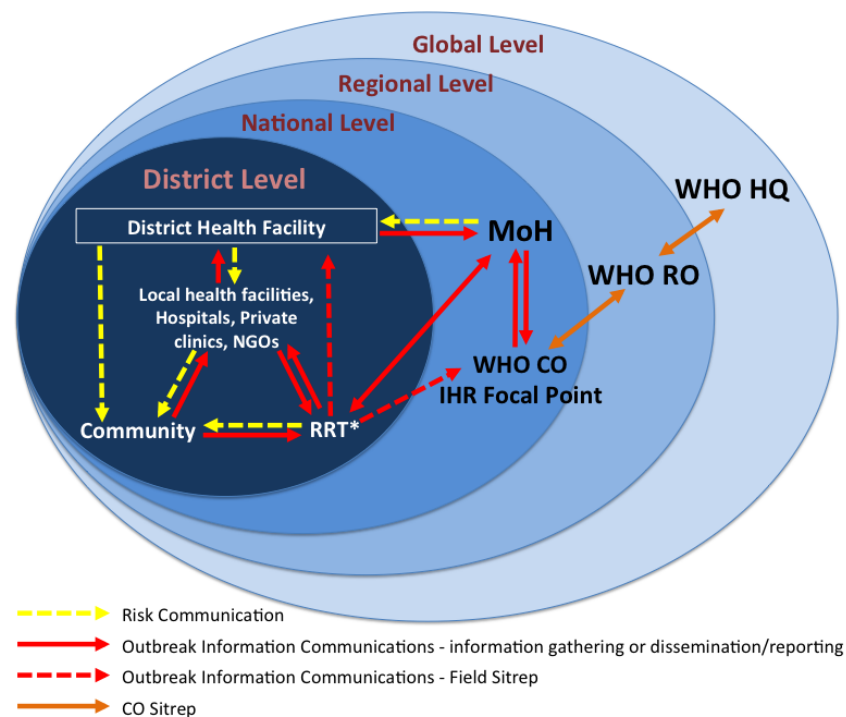
The overall plan should address:

- (a) Communication within the RRT/outbreak investigation team (see Section 4.1.4).
- (b) RRT/outbreak investigation team communication with agencies involved in the outbreak, i.e. WHO country office (CO), local authorities, industry groups, local hospitals, primary healthcare providers, etc. (Section 4.2.3).
- (c) RRT/outbreak investigation team communication with the public, either directly or through the media (Section 4.2.3 – Risk Communication).

- (d) Communication between levels of the health system, with ministries and other government agencies (Section 4.2.3 – Communication within the health system).

### RRT communication

In addition to communication within the RRT (section 4.1.4) the RRT should maintain communication with relevant agencies/stakeholders at the next level above, such as the district health facility or a designated public health emergency management committee, and with the WHO country office (WHO CO) and may be required to provide risk communication to the public. The RRT should provide regular communication about the outbreak to the agency directly above them (District Health Facility) and to the WHO country office in the form of situation reports (sitreps) (Figures 8 and 9). The frequency of these reports may be dictated by the evolution of the outbreak. However, Sitreps are generally communicated daily in an outbreak situation and provide data on the progress of the outbreak investigation (“epi” curves, line lists of cases, etc.), any changes since the last report, foreseeable issues in investigation or response activities, and details of response activities (Annex 8).



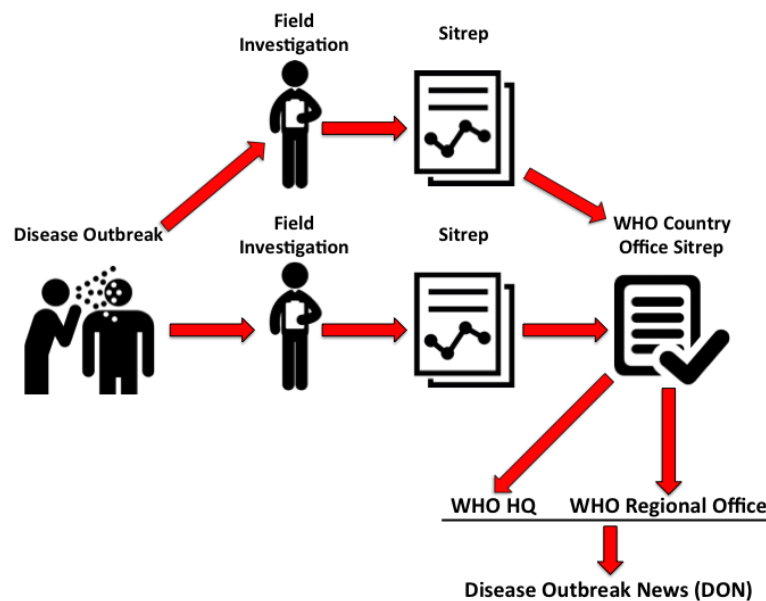
CO = country office  
 HQ = headquarters  
 IHR = International Health Regulations  
 MoH = ministry of health  
 RO = regional office  
 WHO = World Health Organization

**Figure 8.** Information flow during a disease outbreak.

From the district health facility, sitreps are communicated to higher levels in the health system so that progress can be reviewed and actions initiated. The WHO CO acts to receive sitreps from field investigation



teams, compile the pooled information into a more detailed sitrep (Annex 8B) and communicate this to the Regional Office for Africa and the WHO headquarters for dissemination as disease outbreak news (Figure 9).



**Figure 9.** Information flow from the RRT/outbreak investigation team to WHO.

### **Risk communication**

Information about an outbreak – risk communication, may be delivered by different sources such as the ministry of health via national messages, local authorities at the district level or from the RRT. All messages conveyed should be consistent and represent common information. In general, key messages will be developed at the national level and be disseminated to lower levels of the health system to be delivered at the district/local/community level. Even though media engagement may be focused at the national level, a strategy for informing the media at the district level should be developed so as to deliver consistent messages (Figure 8).

Communication with the public in an outbreak is a key component in outbreak control. Therefore, communication strategies should be developed that (i) engage the community to build trust, (ii) deliver transparent, factual, accurate, candid and easily understandable messages, (iii) engage with the community so as to ascertain their concerns and address them and (iv) are planned and delivered in real time. Education messages to deliver to the community should focus on recognition of the disease, how to prevent it and when to seek treatment.

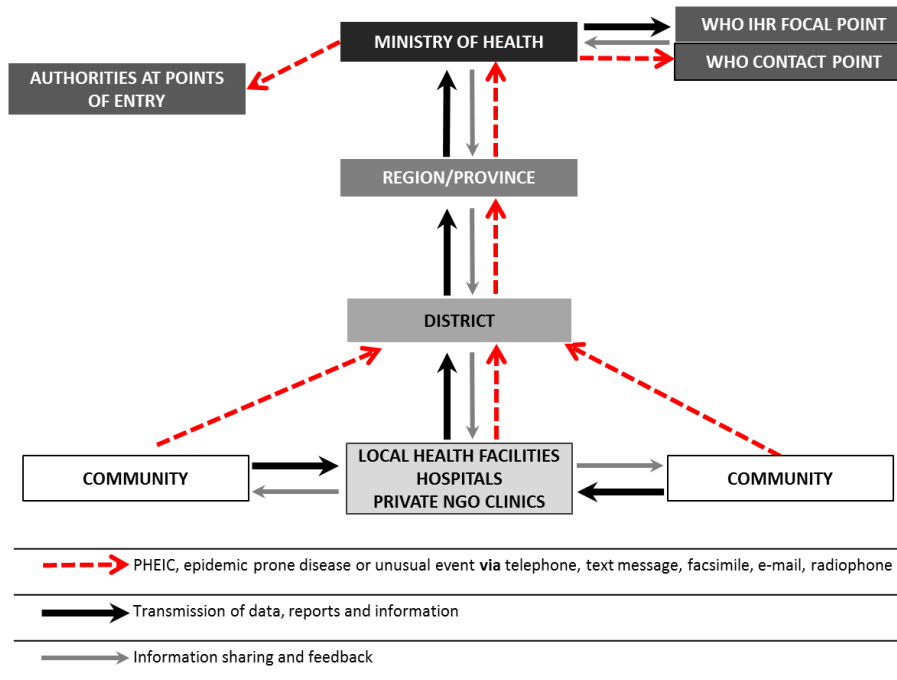
Information dissemination at the district level is a key driver in response and control of an outbreak. Information at the district/community level may be disseminated through the mass media (TV, radio, newspapers), meetings (community, religious and other meetings), distribution of posters and fliers and multimedia presentations such as short films delivered to community groups, at schools, health and/or

religious centres. Activities of relevant personnel identified at the district level should include but are not limited to (30):

- (i) Identifying a spokesperson(s) at district level (political and technical);
- (ii) Liaising regularly with national authorities to provide them with first-hand information (received from the community/local level, from the media or local stakeholders etc.);
- (iii) Be in regular contact with national authorities to receive common messages, including guidelines and answers to frequently asked questions to feed the local media;
- (iv) Being available for interviews with the local media upon request to provide accurate, transparent and up-to-date information following directions from the national level in simple, clear key messages;
- (v) Organizing press briefings to provide regular information to local media, following directions from national level;
- (vi) Developing good relationships with local media so that an effective partnership is established for delivery of accurate, transparent and timely messages to the population;
- (vii) Using information materials developed at the national level with clear, consistent messages to provide guidance to the population;
- (viii) Identifying powerful local channels for the delivery of information to the population;
- (ix) Meet regularly with local stakeholders to disseminate correct messages on disease prevention and surveillance to the population;
- (x) Organize preventive door-to-door campaigns to reach remote rural areas and promote prevention and surveillance of disease, following directions from the national level.

### ***Communication within the health system***

Within the health system Information should flow freely. Communications should be transparent, timely and unambiguous since they are critical for a rapid and effective response and containment of an infectious disease outbreak, which is the preferred outcome. Communication within the health system will encompass information gathering and analysis (number of cases, laboratory data, case locations etc.) and information dissemination, such as media engagement and risk communication messages to both the public/community and healthcare workers (Figures 8 and 10). A suggested flow of information is illustrated in Figure 10.



**Figure 10.** Suggested information flow within a national health system.

### WHO communication resources

WHO. 2005. *Outbreak communication: best practices for communicating with the public during an outbreak*. ([http://www.who.int/csr/resources/publications/WHO\\_CDS\\_2005\\_32/en/](http://www.who.int/csr/resources/publications/WHO_CDS_2005_32/en/)).

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#### 4.2.4 Reporting and notification

##### Reporting

Once the initial investigation has been concluded, the investigation team should conduct a risk assessment to assess the public health risk of the outbreak (46). Based on the assessment and the field investigation findings, the team should prepare a report that details the characteristics of the outbreak and any conclusions as to the disease etiology, source, mode of transmission, population(s) affected etc. and disseminate it immediately to the entity that engaged the RRT/outbreak investigation team, relevant health facilities, other relevant agencies and stakeholders. A sample report outline is provided in Annex 9.

##### IHR notification

The IHR decision instrument (Annex 7A) can be used to determine if an event is to be reported to the WHO under the IHR (2005) regulations. Further guidance on the use of the IHR decision instrument, including examples of its application can be found in Annex 7B (47).

## **4.3 Investigation control measures**

### **4.3.1 Case management**

Priority should be given to those who are sick in management of the symptoms and in case the etiology is suspected but not confirmed, then available treatments should be considered presumptively. Signs, symptoms and clinical progression should be recorded and information about management procedures that appear to be effective should be shared with other healthcare workers in the outbreak location. For emerging respiratory infections of unknown etiology, healthcare workers are particularly at risk and PPE should be available and used rigorously. In healthcare facilities, emphasis should not only be placed on PPE but also on source, administrative, environmental and engineering controls. Additionally, the ministry of health should make available standard operating procedures (SOPs) or guidelines for the case management of individuals with severe acute respiratory infection (SARI), which may be further adapted for the outbreak using available reference material (e.g. WHO interim guidance used on clinical management of severe acute respiratory infection when Middle East respiratory syndrome coronavirus (MERS-CoV) infection is suspected (48)). Furthermore, isolation facilities, equipped with negative pressure rooms, should be available to ensure safe and appropriate treatment of SARI patients infected with highly pathogenic agents. For further information, see WHO Guidelines *Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections* (35).

### **4.3.2 Preventing further transmission**

Public health interventions that can be used to prevent further disease transmission depend on the suspected etiology, source and modes of transmission. As can be seen from Box 1 below, a variety of interventions are available and they can be directed at the source or individuals at risk of infection (Box 1).

When the source and modes of transmission are unknown for a respiratory disease outbreak, a precautionary approach should be applied in attempting to stop transmission. Social distancing measures such as school closures, avoidance of suspected food sources or culling of animals may be required. These measures require coordination with relevant intersectoral authorities, are difficult to implement and monitor, and can be costly to those affected. Therefore, instigating such measures mandates careful consideration and consultation, and their impact should be regularly assessed, reviewed and modified based on increasing evidence about the outbreak.

### **4.3.3 Monitoring the response**

Active surveillance, routine data analysis, and frequent communication and feedback to clinicians, public health teams, the community and other identified stakeholders are integral until the outbreak is contained. Updated case and clinical data, outbreak magnitude, laboratory findings and effective prevention measures should be shared routinely, especially for emerging infections for which the evidence-base is yet to be

established. An outbreak can be deemed contained if active surveillance in the at-risk population has not yielded new cases during two-times the presumed incubation period for that infection.

**Box 1:** Public health interventions to prevent transmission and spread of an outbreak

**Interventions directed at the source:**

- Treat infected person using antibiotics or antiviral agents;
- Isolate infected persons;
- Quarantine exposed persons or contaminated sites/sources;
- Involve animal health authorities for relevant control measures if animal source identified;
- Implement cordon sanitaire, prevent mass gatherings and limit people's movement;
- Involve food safety authorities for relevant control measures if food source identified;
- Clean and disinfect contaminated surfaces or environments;
- Modify behaviour, such as wearing of surgical mask;
- Deter through civil or criminal prosecution.

**Interventions directed at susceptible individuals:**

- Administer prophylaxis;
- Vaccinate;
- Use barrier nursing techniques;
- Implement cordon sanitaire, prevent mass gatherings and limit people's movement;
- Modify behaviour, such as increased hand washing;
- Use shelter-in-place (reverse quarantine);
- Trace and monitor contacts;
- Communicate prevention strategies through media or health alerts/notices.

Source: Adapted from (39).

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## Annexes

### Annex 1. Known etiological agents of acute respiratory infections

A number of organisms, including bacteria and viruses can cause acute respiratory infections (ARIs). The majority of agents, such as rhinovirus or adenovirus, cause mild respiratory disease that is often self-limiting and does not progress to more severe respiratory disease requiring hospitalization. However, a number of agents can cause severe respiratory disease that can result in hospitalization and death. It should also be noted that progression of disease may depend on age, (children under 5 years and adults over 65 years increased susceptibility), immune status and co-morbidities. Immunocompromised individuals and those with serious co-morbidities are the most vulnerable to severe disease.

**Table A1.** Common communicable viral and bacterial agents causing acute respiratory infections

Viral causes of ARI	Clinical syndrome *	Outbreaks (year and location)	Reference
Influenza A and B	Influenza like illness Pneumonia Bronchiolitis Common cold Croup	2002 – seasonal influenza; Democratic Republic of the Congo and Madagascar 2009 – pandemic influenza A(H1N1)pdm09 2013–present – avian influenza A(H7N9), China	(49, 50)  (51)
Respiratory syncytial virus (RSV)	Bronchiolitis Pneumonia Common cold Croup Influenza-like illness	2011, Republic of Korea 2014, Japan	(52) (53)
Adenovirus	Pneumonia Bronchiolitis Common cold Croup Influenza like illness	2008–2009, China 2013, China	(54) (55)
Human coronaviruses (229E, OC43, HKU1, NL63)	<b>Common cold</b> Pneumonia	No outbreaks to date	–
SARS coronavirus SARS-CoV	<b>Pneumonia</b>	2003/2004, China, Hong Kong SAR, Vietnam, Canada and Singapore	(56)
MERS coronavirus MERS-CoV	<b>Pneumonia</b>	2012–2015, Saudi Arabia and Middle East countries	(57)
Parainfluenza 1, 2 and 3	<b>Croup</b> Bronchiolitis Common cold Influenza like illness Pneumonia	No significant outbreaks to date	–
Human metapneumovirus	<b>Bronchiolitis</b> <b>Pneumonia</b> Common cold Pneumonia	2011/2012, USA 2010, United Kingdom	(58) (59)
Enteroviruses Rhinovirus EV-D68 <sup>#</sup>	<b>Common cold</b> Bronchiolitis Pneumonia	Rhinovirus: 2007/2008, Vietnam EV-D68: 2014, USA, France	(60) (61),(62)

Viral causes of ARI	Clinical syndrome *	Outbreaks (year and location)	Reference
Hantavirus pulmonary syndrome	<b>Respiratory symptoms</b> (4–10 days after initial symptoms) coughing and shortness of breath	2009/2010, Brazil 2012, USA (Yosemite National Park)	(63) (64)
<b>Bacterial causes of ARI</b>	<b>Clinical Syndrome</b>	<b>Outbreaks</b>	
<i>Klebsiella pneumoniae</i>	Pneumonia	Community acquired pneumonias, may be secondary to viral infections	–
<i>Haemophilus influenzae</i>	Pneumonia		
<i>Staphylococcus aureus</i>	Pneumonia		
<i>Streptococcus pneumoniae</i>	Pneumonia	2006, United Kingdom 2005/2006, Israel	(65) (66)
<i>Mycoplasma pneumoniae</i>	Pneumonia, tracheobronchitis, pharyngitis	2014, USA (Nebraska)	(67)
<i>Mycoplasma tuberculosis</i>	Pneumonia	Ongoing cases globally	
Diphtheria <i>Corynebacterium diphtheriae</i>	Pharyngitis	2011, Nigeria	(68)
Whooping cough <i>Bordetella pertussis</i>	Paroxysms (fits, rapid coughs followed by a high-pitched “whoop”	2003, Afghanistan Ongoing cases globally	(69)
Pneumonic plague <i>Yersinia pestis</i>	Pneumonia	2014/2015, Madagascar	(70)
Scarlet fever <i>Streptococcus pyogenes</i> Group A Streptococcus	Pharyngitis	Ongoing cases globally	–

\* Bold type indicates that the agent is a common cause of the syndrome.

# Predominantly affects children, causes wheezing and difficulty breathing.

## Annex 2. Case definitions for known respiratory diseases

African Region IDSR priority diseases		
Respiratory disease agent	Community level key signs and symptoms	Case definition
<b>Viral</b>		
SARI* (≥ 5 years old)		<p>Any severely ill person presenting with an acute respiratory infection with:</p> <ul style="list-style-type: none"> <li>• History of fever or measured fever of ≥38°C or higher <b>and</b></li> <li>• Cough with onset within the last 10 days <b>and</b></li> <li>• Required hospitalization</li> </ul>
Influenza by new subtype <sup>#</sup>		<p><b>Suspected H5N1 case:</b> Any person presenting with unexplained acute lower respiratory illness with fever (≥38°C) and cough, shortness of breath or difficulty breathing <b>and</b> one or more of the following exposures in the 7 days prior to symptom onset:</p> <ul style="list-style-type: none"> <li>• Close contact (within 1 meter) with a person (e.g. caring for, speaking with, or touching) who is a suspected, probable or confirmed A(H5N1) case;</li> <li>• Exposure (e.g. handling, slaughtering, de-feathering, butchering, preparing for consumption) to poultry or wild birds or their remains or to environments contaminated by their faeces in an area where A(H5N1) infections in animals or humans have been suspected or confirmed in the last month;</li> <li>• Consumption of raw or undercooked poultry products in an area where A(H5N1) infections in animals or humans have been suspected or confirmed in the last month; Close contact with a confirmed A(H5N1) infected animal other than poultry or wild birds;</li> <li>• Handling of animal or human samples suspected to contain A(H5N1) virus in a laboratory or other setting.</li> </ul> <p><b>Confirmed A(H5N1) case:</b> A person meeting the criteria for a suspected case <b>and</b> positive laboratory results from a laboratory whose A(H5N1) test results are accepted by WHO as confirmatory.</p> <p><b>Suspected pandemic (H1N1)pdm09 virus infection:</b> An individual presenting with influenza-like illness (sudden onset of fever &gt; 38 °C and cough or sore throat, in the absence of another diagnosis) with a history of exposure to a pandemic A(H1N1)pdm09 virus.</p> <p><b>Confirmed pandemic A(H1N1)pdm09 virus infection:</b> An individual with a laboratory-confirmed pandemic A(H1N1)pdm09 virus infection by one or more of the following tests: PCR; viral culture; 4-fold rise in pandemic A(H1N1)pdm09 virus-specific neutralizing antibodies.</p>
SARS <sup>#</sup>		<p><b>Suspected case of SARS:</b> An individual with:</p> <p>A history of fever or documented fever ≥ 38 °C <b>and</b></p> <ul style="list-style-type: none"> <li>• One or more symptoms of lower respiratory tract illness: cough, difficulty breathing and shortness of breath <b>and</b></li> <li>• Radiographic evidence of lung infiltrates consistent with</li> </ul>

		<p>pneumonia or ARDS or autopsy findings consistent with the pathology of pneumonia or ARDS without an identifiable cause <b>and</b></p> <ul style="list-style-type: none"> <li>No alternative diagnosis can fully explain the illness.</li> </ul> <p><b>Confirmed case of SARS:</b> An individual who tests positive for SARS-CoV infection by the WHO recommended testing procedures.</p>
MERS <sup>^</sup>		<p><b>Probable MERS case:</b></p> <ul style="list-style-type: none"> <li>A febrile acute respiratory illness with clinical, radiological or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or acute respiratory distress syndrome) <b>and</b></li> <li>Direct epidemiologic link<sup>2</sup> with a confirmed MERS-CoV case <b>and</b></li> <li>A negative or inconclusive laboratory diagnosis on a single inadequate specimen or testing for MERS-CoV is unavailable.<sup>3</sup></li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>A febrile acute respiratory illness with clinical, radiological or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or acute respiratory distress syndrome) <b>and</b></li> <li>The person resides in or travelled to the Middle East or countries where MERS-CoV is known to be circulating in dromedary camels or where human infections have recently occurred <b>and</b></li> <li>Testing for MERS-CoV is inconclusive.</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>An acute febrile respiratory illness of any severity <b>and</b></li> <li>Direct epidemiologic link<sup>2</sup> with a confirmed MERS-CoV case <b>and</b></li> <li>Testing for MERS-CoV is inconclusive</li> </ul> <p><b>Confirmed MERS case</b></p> <ul style="list-style-type: none"> <li>A person with laboratory confirmed MERS-CoV infection irrespective of clinical signs and symptoms.</li> </ul>
<b>Bacterial</b>		
Pulmonary (inhalation) Anthrax <sup>#</sup> <i>Bacillus anthracis</i>		<p><b>Suspected case:</b> Any person with acute disease onset characterized by:</p> <ul style="list-style-type: none"> <li>A brief prodrome resembling acute viral respiratory illness followed by rapid onset of hypoxia, dyspnoea and high temperature, with X-ray evidence of mediastinal widening <b>and</b></li> <li>An epidemiological link to confirmed or suspected animal cases or contaminated animal products.</li> </ul> <p><b>Confirmed case:</b> A confirmed case of anthrax in a human can be defined as a clinically compatible case of cutaneous, inhalational or gastrointestinal illness that is laboratory confirmed by</p> <ul style="list-style-type: none"> <li>Isolation of <i>B. anthracis</i> from an affected tissue or site or</li> <li>Other laboratory evidence of <i>B. anthracis</i> infection based on at least two supportive laboratory tests.</li> </ul>
Pneumonic plague <sup>#</sup>	In an area known to have plague, any	<p><b>Suspected case:</b> Any person with</p> <ul style="list-style-type: none"> <li>Sudden onset of fever, chills, headache, severe malaise,</li> </ul>

<p><i>Yersinia pestis</i></p>	<p>person with cough, chest pain and fever</p>	<p>prostration and very painful swelling of lymph nodes, <b>or</b></p> <ul style="list-style-type: none"> <li>• Cough with blood stained sputum, chest pain and difficulty breathing.</li> </ul> <p><b>Confirmed case:</b> Suspected case confirmed by</p> <ul style="list-style-type: none"> <li>• Isolation of <i>Yersinia pestis</i> from blood <b>or</b></li> <li>• Aspiration of buboes <b>or</b></li> <li>• Epidemiologic link to confirmed cases or outbreak</li> </ul>
<p>Tuberculosis<sup>#</sup> <i>Mycoplasma tuberculosis</i></p>	<p>Any person with cough lasting 3 weeks or more</p>	<p><b>Suspected case:</b> Any person with a cough of 3 weeks or more.</p> <p><b>Confirmed case:</b> <b>Smear positive Pulmonary TB (PTB):</b></p> <ul style="list-style-type: none"> <li>• A suspected patient with at least two sputum specimens positive for acid-fast bacilli (AFB) <b>or</b></li> <li>• One sputum specimen positive for AFB by microscopy and radiographic abnormalities consistent with active PTB as determined by the treating medical officer, <b>or</b></li> <li>• One positive sputum smear by microscopy and one sputum specimen positive on culture for AFB.</li> </ul> <p><b>Smear negative PTB:</b> A patient who fulfils the following criteria:</p> <ul style="list-style-type: none"> <li>• Two sets taken at least two weeks apart of at least two sputum specimens negative for AFB on microscopy, radiographic abnormalities consistent with PTB, and a lack of clinical response despite one week of a broad spectrum antibiotic, a decision by a physician to treat with a full course of anti-TB chemotherapy, <b>or</b></li> <li>• A patient who fulfils all the following criteria: severely ill, at least two sputum specimens negative for AFB by microscopy, radiographic abnormalities consistent with extensive pulmonary TB (interstitial and miliary) a decision by a physician to treat with a full course of anti-TB chemotherapy, <b>or</b></li> <li>• A patient whose initial sputum smears were negative, who had sputum sent for culture initially, and whose subsequent sputum culture result is positive.</li> </ul>
<p><b>Other</b></p>		
<p>Severe pneumonia in children under 5 years<sup>#</sup></p>	<p>Any child less than 5 years of age with cough and fast breathing or difficulty in breathing</p>	<p><b>Clinical case definition (Integrated Management of Childhood Illness, IMCI) for pneumonia:</b> A child presenting with cough or difficult breathing and:</p> <ul style="list-style-type: none"> <li>• 50 or more breaths per minute for infant aged 2 months to 1 year</li> <li>• 40 or more breaths per minute for young child aged 1 year up to 5 years.</li> </ul> <p><b>Note:</b> A young infant aged 0 up to 2 months with cough and fast breathing is classified in IMCI as “serious bacterial infection” and is referred for further evaluation.</p> <p><b>Clinical case definition (IMCI) for severe pneumonia:</b></p> <ul style="list-style-type: none"> <li>• A child presenting with cough or difficulty breathing and any general danger sign, or chest in-drawing, or stridor in a calm child. General danger signs for children 2 months to 5 years are: unable to drink or breast feed, vomits everything, convulsions, lethargy, or unconsciousness.</li> </ul>



Outbreak associated agents causing ARI		
Viral		
ILI Influenza-like illness*	Any person with fever and cough or sore throat or nasal discharge	<b>An acute respiratory infection with:</b> <ul style="list-style-type: none"> <li>• Measured fever of <math>\geq 38^{\circ}\text{C}</math> <b>and</b></li> <li>• Cough with onset within the 10 days</li> </ul>
RSV <sup>±</sup>		<b>Severe RSV LRTI (infant)</b> <b>Clinical criteria</b> <ul style="list-style-type: none"> <li>• Respiratory infection defined as a cough or difficulty breathing</li> </ul> <b>and</b> <ul style="list-style-type: none"> <li>• LRTI, defined as fast breathing by WHO criteria <b>or</b> SpO2 &lt; 95%, and</li> <li>• <math>\geq 1</math> of the following features of severe disease: pulse oximetry &lt; 93%, lower chest wall in-drawing</li> </ul> <b>Very severe RSV LRTI (infant)</b> <b>Clinical criteria</b> <ul style="list-style-type: none"> <li>• Respiratory infection defined as cough or difficulty breathing <b>and</b></li> <li>• LRTI, defined as fast breathing by WHO criteria <b>or</b> SpO2 &lt; 95% <b>and</b></li> <li>• One or more of the following features of very severe disease: pulse oximetry &lt; 90%, inability to feed, and failure to respond/unconsciousness.</li> </ul>
Hantavirus pulmonary syndrome <sup>‡</sup>		<b>Clinical case description</b> <ul style="list-style-type: none"> <li>• Acute febrile illness temperature greater than <math>38.3^{\circ}\text{C}</math> with a prodrome consisting of fever, chills, myalgia, headache, and gastrointestinal symptoms, and one or more of the following clinical features: bilateral diffuse interstitial oedema <b>or</b></li> <li>• Clinical diagnosis of acute respiratory distress syndrome (ARDS) <b>or</b></li> <li>• Radiographic evidence of noncardiogenic pulmonary oedema <b>or</b></li> <li>• An unexplained respiratory illness resulting in death, and includes an autopsy examination demonstrating noncardiogenic pulmonary oedema without an identifiable cause <b>or</b></li> <li>• Healthcare record with a diagnosis of hantavirus pulmonary syndrome <b>or</b></li> <li>• Death certificate listing hantavirus pulmonary syndrome as cause of death or a significant condition contributing to death</li> </ul>
Bacterial		
Diphtheria <sup>+</sup>		An illness characterized by laryngitis <b>or</b> pharyngitis <b>or</b> tonsillitis <b>and</b> An adherent membrane of the tonsils, pharynx and/or nose
Legionnaires' disease <sup>‡</sup>		<b>Clinical description</b> Disease characterized by fever, myalgia, cough and clinical or radiographic pneumonia
Pertussis		<b>Clinical case definition</b> A case diagnosed as pertussis by a physician <b>or</b> Person with a cough lasting at least 2 weeks, with at least one of the symptoms: <ul style="list-style-type: none"> <li>• Paroxysms (i.e. fits) of coughing,</li> <li>• Inspiratory whooping</li> <li>• Post-tussive vomiting (i.e. vomiting immediately after coughing) and without other apparent cause</li> </ul>



Scarlet fever <sup>‡</sup> <i>Streptococcus pyogenes</i> (GAS)		<b>Common clinical symptoms</b> <ul style="list-style-type: none"> <li>• A very red sore throat</li> <li>• Fever (<math>\geq 38</math> °C)</li> <li>• A red rash with a sandpaper feel</li> <li>• Bright red skin in underarm, elbow and groin creases</li> <li>• A whitish coating on the tongue or back of the throat</li> <li>• A “strawberry” tongue</li> <li>• Headache</li> <li>• Nausea or vomiting</li> <li>• Abdominal pain</li> <li>• Swollen glands</li> <li>• Body aches</li> </ul>
Streptococcal pharyngitis GAS		<b>Common clinical symptoms</b> <ul style="list-style-type: none"> <li>• Sore throat, usually starts quickly and can cause severe pain when swallowing</li> <li>• Fever (<math>\geq 38</math> °C)</li> <li>• Red and swollen tonsils, sometimes with white patches or streaks of pus</li> <li>• Tiny red spots (petechiae) on the area at the back of the roof of the mouth (the soft or hard palate)</li> <li>• Headache, nausea or vomiting</li> <li>• Swollen lymph nodes in the neck</li> <li>• Body aches or rash</li> </ul>

\* (71), # (30), ^ (72), <sup>δ</sup> (73), <sup>‡</sup> CDC – [www.cdc.gov](http://www.cdc.gov), <sup>β+</sup> (74)

### Annex 3. Health structures' roles and responsibilities

Site	Role	Expertise
National level of health system, e.g. surveillance unit in ministry of health OR National level of agricultural and/or animal health system, e.g. surveillance unit in ministry of agriculture	<ul style="list-style-type: none"> <li>Develop/adapt guidelines, policies and procedures for the analysis and interpretation of data, case management and national laboratory networks;</li> <li>Report diseases and events to the appropriate authorities immediately and share information with regional and international networks;</li> <li>Coordinate and collaborate with international authorities;</li> <li>Support epidemic response activities and provide logistical support for outbreak activities including deployment of RRT;</li> <li>Oversee laboratory involvement, ensuring that requests for additional specimens and transfer of specimens to reference laboratories are implemented;</li> <li>Response coordination;</li> <li>Data management.</li> </ul>	<p>Epidemiologists</p> <p>Data managers</p> <p>RRT leaders</p> <p>Communication officers</p> <p>Veterinarians (MoA)</p> <p>Wildlife experts (MoA)</p> <p>Logisticians</p>
District, state and provincial levels of the health system	<ul style="list-style-type: none"> <li>Collect and analyse outbreak data, both laboratory and epidemiological (time, place and person) data;</li> <li>Report epidemiological and laboratory data to next level;</li> <li>Ensure compliance of healthcare facilities with respect to case definitions and case reporting procedures;</li> <li>Arrange and lead investigations into outbreak;</li> <li>Select and implement appropriate public health responses to outbreak;</li> <li>Oversee procedures for specimen collection, packaging and transport.</li> </ul>	<p>Epidemiologists</p> <p>Laboratory technicians</p> <p>Data managers</p> <p>RRT leaders</p>
Reference laboratories for viral respiratory diseases (influenza reference lab)	<ul style="list-style-type: none"> <li>Detect respiratory pathogens in samples from suspected cases, in particular influenza viruses;</li> <li>Provide protocols and materials for shipping of samples locally and internationally;</li> <li>Transfer clinical specimens or viral isolates to reference laboratories.</li> </ul>	<p>Laboratory scientists and technicians</p>
Hospital/health facility including influenza sentinel sites	<ul style="list-style-type: none"> <li>Detect cases of respiratory infection (case-finding);</li> <li>Collect and transport specimens to laboratory;</li> <li>Report case-based information, laboratory results, etc. to appropriate level in health system;</li> <li>Take part in outbreak investigation;</li> <li>Case management – cases and contacts;</li> <li>Implement control measures.</li> </ul>	<p>Clinicians</p> <p>Nurses</p> <p>Healthcare workers</p> <p>Infection control specialists</p>

Site	Role	Expertise
Community	<ul style="list-style-type: none"> <li>• Identify events and conditions in the community (case identification);</li> <li>• Report events/cases to appropriate authorities in health system;</li> <li>• Assist in outbreak investigation activities at community level;</li> <li>• Assist in response activities;</li> <li>• Implement community-based education.</li> </ul>	<p>Local leaders</p> <p>Primary health care workers</p>

Source: adapted from (75)

## Annex 4. Composition, roles and responsibilities of members of RRT

In general, the roles and responsibilities of a RRT in the initial phase of a disease outbreak include:

- (a) Investigate the reported outbreak or rumours of outbreaks and other public health emergencies.
- (b) Advise on appropriate measures to control the outbreak, including risk communication activities and initiate implementation of control measures including capacity building.
- (c) Coordinate rapid response activities with other stakeholders. The RRT may operate in conjunction with and benefit from support through the emergency operations centre (EOC), which serves as a hub for coordination, communication and information management during public health emergencies.

Membership of the RRT should reflect the technical expertise required for the outbreak investigation and response.

The following table is not an exhaustive list of the skills, roles or responsibilities of members of an RRT. A comprehensive list can be found in *Public health events of initially unknown etiology: A framework for preparedness and response in the African Region*.

Team member	Preferred skills	Key responsibilities in outbreak investigation
Team leader	<ul style="list-style-type: none"> <li>• Management or team leadership;</li> <li>• Experience with outbreak response</li> <li>• Experience with disease surveillance and response (IDSR/IHR, One Health approach)</li> <li>• Ability to engage technical and political entities within the national government</li> <li>• Demonstrated leadership qualities;</li> <li>• Ability to advocate for and mobilize resources from technical and political bodies.</li> </ul>	<ul style="list-style-type: none"> <li>• Maintain communication with and work in coordination with multisectoral institutions, partners and members of RRT</li> <li>• Ensure that both technical and political mechanisms respond appropriately to the disease outbreak</li> <li>• Oversee the technical activities of each RRT member</li> <li>• With the epidemiologist, oversee the management and interpretation of all RRT-generated data.</li> </ul>
Human and/or animal epidemiologist	<ul style="list-style-type: none"> <li>• Qualifications and experience in field epidemiology</li> <li>• Field experience in responding to infectious disease outbreaks</li> </ul>	<ul style="list-style-type: none"> <li>• Investigate and analyse epidemiology of clusters of suspected, probable or confirmed illnesses for factors of time, place, person and mode of disease transmission, as well as to determine the etiology of the disease outbreak</li> <li>• Establish or strengthen active disease surveillance activities and follow up on case contacts</li> <li>• With the manager or team leader, oversee the determination and interpretation of recommended indicators</li> <li>• Working with the team leader, support mobilization of field teams for rapid outbreak assessment or investigation;</li> <li>• Evaluate the current alert and response systems, including existing case definitions</li> <li>• Supervise data management, analysis and interpretation</li> <li>• Lead the planning of the strategy and methods to determine the etiology of the</li> </ul>

Team member	Preferred skills	Key responsibilities in outbreak investigation
		<p>illness during a PHE</p> <ul style="list-style-type: none"> <li>• Ensure clear routine reporting of key information to stakeholders at national, district or provincial level</li> <li>• Liaise with international partners in the field to facilitate field investigations;</li> <li>• Identify the factors in the occurrence of the PHE in question</li> <li>• Update and share surveillance data with the rest of the team</li> <li>• Set in motion mechanisms to break the contamination chain for infectious diseases.</li> </ul>
Clinician and/or infection prevention and control expert	<ul style="list-style-type: none"> <li>• Medical or nursing qualification</li> <li>• Field experience in clinical case management</li> <li>• Clinical and/or field experience in infection control</li> </ul>	<ul style="list-style-type: none"> <li>• Directly support proper case management and provision of optimum care for cases in health facilities and the community</li> <li>• Provide guidance on clinical and epidemiological case definitions</li> <li>• Collect robust demographic, treatment, and patient monitoring data for improved clinical response to PHEs</li> <li>• Assess infection control practices in healthcare facilities in affected areas</li> <li>• Provide guidance on the necessary infection control equipment for central, provincial and district level hospitals and facilities during a PHE</li> <li>• Review and where appropriate recommend changes to update infection control guidelines based on lessons learnt at healthcare facilities during PHEs</li> <li>• Conduct appropriate on-site infection prevention and control training for staff at provincial or district hospitals after reviewing local infection control measures</li> <li>• Coordinate work with all the response teams</li> <li>• Report on findings of investigations and assist the RRT or international team and national authorities to formulate a plan of action, and participate in after-action reviews.</li> </ul>
Laboratory expert	<ul style="list-style-type: none"> <li>• Qualification in microbiology, biology or a related laboratory science</li> <li>• Experience and/or knowledge of specimen collection, storage and shipping, biosafety/biosecurity and networking of public health laboratories for surveillance and response to outbreak-prone diseases.</li> </ul>	<ul style="list-style-type: none"> <li>• Provide guidance in the establishment of a system for safe and appropriate collection, packaging and transport of samples from the field to the reference laboratory</li> <li>• Develop/adapt and facilitate the implementation of standard operating procedures for participation of laboratories in investigation and laboratory confirmation of PHEs</li> <li>• Support setting up of mobile laboratories if required</li> </ul>

Team member	Preferred skills	Key responsibilities in outbreak investigation
		<ul style="list-style-type: none"> <li>Facilitate collaboration with other disciplines if required, based on laboratory results.</li> </ul>
Veterinary/wildlife expert	<ul style="list-style-type: none"> <li>Qualification in veterinary or wildlife science</li> <li>Experience in animal health and zoonoses, in particular disease detection and reporting</li> <li>Knowledge of domestic and wild animal pathologies</li> </ul>	<ul style="list-style-type: none"> <li>Manage diagnostic activities for animal diseases, including materials and/or sampling</li> <li>Oversee the application of biosecurity measures if required</li> <li>Lead information analysis and investigation in the event of a suspected outbreaks affecting animals</li> <li>Guide epidemic control measures for animal disease vectors</li> <li>Assess household practices for animals to maximize the effectiveness of disease control efforts</li> <li>Define the relationship between pathogenic agents and hosts and the environment: parasitism, commensalism: symbiosis</li> <li>Ensure proper expertise about bush meat and safe butchering, handling and preparation</li> <li>Determine the relationship between different disease factors: vectors, reservoirs, hosts.</li> </ul>
Social mobilization expert	<ul style="list-style-type: none"> <li>Qualification in social sciences or communication;</li> <li>Experience in social mobilization or behavioural communication approaches</li> </ul>	<ul style="list-style-type: none"> <li>Undertake rapid appraisals to understand perceptions, knowledge, beliefs and practices within households, communities and healthcare settings in affected areas in relation to the outbreak and its control, prevention, and treatment interventions</li> <li>Identify barriers and facilitating factors that may affect the uptake of recommended risk reduction and health protection measures within households, communities and healthcare settings</li> <li>Advise and make recommendations on the design and implementation of effective communication strategies and interventions and develop social mobilization strategies that support outbreak control and prevention</li> </ul>
Logistician	<ul style="list-style-type: none"> <li>Field experience in logistical operations in responding to infectious disease outbreaks</li> </ul>	<ul style="list-style-type: none"> <li>Ensure logistical support is provided for investigation of and response to disease outbreak</li> <li>Maintain stockpiles of essential materials such as personal protective equipment</li> <li>Provide logistical support for tracking shipment of samples to identified laboratories</li> <li>Look after logistical communication devices</li> <li>Coordinate team security</li> </ul>

Source: Adapted from (75).

## Annex 5. Guidelines for use of PPE

For the safe collection of specimens from infected individuals the following procedures should be adopted in regards to personal protective equipment (PPE). In situations where the etiology is unknown, maximum precautions and protection should be applied to minimize the risk of infection.

Personal protection	Use	Requirements	Viral pathogens
<b>Standard</b>	Standard IPC precautions	<ul style="list-style-type: none"> <li>• Hand hygiene</li> <li>• Gloves</li> <li>• Gown</li> <li>• Eye protection (goggles or face shield)</li> <li>• Medical mask if performing aerosol-generating procedures or activities that may result in splashes or sprays of blood, body fluids, secretions and or excretions, <b>or</b> if in close contact with a patient who has respiratory symptoms such as cough or sneezing.</li> </ul>	
<b>Droplet</b>		<ul style="list-style-type: none"> <li>• Standard precautions</li> <li>• Medical mask if within 1 m of patient</li> </ul>	<ul style="list-style-type: none"> <li>• Adenovirus</li> <li>• Avian influenza A(H5N1)</li> <li>• Human influenza</li> <li>• SARS-CoV</li> </ul>
<b>Contact</b>	For patients known or suspected to have serious illnesses easily transmitted by direct patient contact or by contact with items in the patient's environment	<ul style="list-style-type: none"> <li>• Hand hygiene</li> <li>• Gloves</li> <li>• Gown (impermeable and disposable. If not impermeable wear an apron)</li> </ul>	<ul style="list-style-type: none"> <li>• Parainfluenza</li> <li>• RSV</li> <li>• Avian influenza A(H5N1)</li> <li>• SARS-CoV</li> </ul>
<b>Airborne</b>	For patients known or suspected to have serious illnesses transmitted by airborne droplet nuclei	<ul style="list-style-type: none"> <li>• Standard precautions</li> <li>• Particulate respiratory mask that is at least as protective as a NIOSH-certified N95, EU FFP2 or equivalent</li> </ul>	<ul style="list-style-type: none"> <li>• SARS-CoV</li> <li>• Human influenza</li> <li>• Other viral respiratory pathogens</li> </ul>

Level of IPC	Infectious agent						
	No pathogen identified, no risk factor for TB or ARI of potential concern (e.g. influenza-like illness without risk factor for ARI of potential concern)	Bacterial ARI, <sup>a</sup> including plague	Other ARI viruses (e.g. parainfluenza RSV, adenovirus)	Influenza virus with sustained human-to-human transmission (e.g. seasonal influenza, pandemic influenza)	New influenza virus with no sustained human-to-human transmission (e.g. avian influenza) <sup>b</sup>	SARS	Novel respiratory infection (route of transmission unknown)
Standard	✓	✓	✓	✓	✓	✓	✓
Droplet	✓		✓	✓	✓	✓	✓
Contact			✓	-	✓	✓	✓
Airborne				-	-	✓	✓

ARI = acute respiratory infection, RSV = respiratory syncytial virus, SARS = severe acute respiratory syndrome, TB = tuberculosis

<sup>a</sup> Bacterial ARI refers to common bacterial respiratory infections caused by organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Chlamydia* spp. and *Mycoplasma pneumoniae*.

<sup>b</sup> As of the publication of (37), no sustained efficient human to human transmission of avian influenza A(H5N1) is known to have occurred, and available evidence does not suggest airborne human to human transmission. Therefore a medical mask is adequate for routine care.

Source: Adapted from (37).



## Annex 6 Supplies and equipment checklists for an outbreak investigation

### Annex 6A Checklist for personal protection equipment (PPE) for outbreak investigation

PPE	
Gowns (impermeable)	<input type="checkbox"/>
Coveralls	<input type="checkbox"/>
Head cover	<input type="checkbox"/>
Eye protection (goggles or face shield)	<input type="checkbox"/>
Rubber gloves	<input type="checkbox"/>
Mask, N95	<input type="checkbox"/>
Boot cover	<input type="checkbox"/>
Examination gloves (S, M, L and XL)	<input type="checkbox"/>
Plastic apron (reusable)	<input type="checkbox"/>
Gum boots <sup>#</sup>	<input type="checkbox"/>
Hand sprayer	<input type="checkbox"/>
Back-pack sprayer	<input type="checkbox"/>
Specimen containers	<input type="checkbox"/>
Packing tape/Scotch tape	<input type="checkbox"/>
Anti-fog for goggles	<input type="checkbox"/>
Chlorine <sup>#</sup>	<input type="checkbox"/>

#### Notes

<sup>#</sup> Can be purchased locally

Source: Adapted from Annex 4C in (30).

## Annex 6B Checklist for laboratory supplies required for specimen collection

<b>Blood collection</b>	
Sterile needles	<input type="checkbox"/>
Sterile syringes	<input type="checkbox"/>
Vacutainers	<input type="checkbox"/>
Test tubes for serum	<input type="checkbox"/>
Antiseptic skin disinfectant	<input type="checkbox"/>
Tourniquets	<input type="checkbox"/>
Transport tubes with screw-on tops	<input type="checkbox"/>
Transport media	<input type="checkbox"/>
Band Aids/bandage	<input type="checkbox"/>
<b>Respiratory specimens</b>	
Viral transport medium (VTM) tubes	<input type="checkbox"/>
Pernasal swabs (sterile, plastic shaft)	<input type="checkbox"/>
Dacron or rayon swabs (sterile, plastic shaft)	<input type="checkbox"/>
Biohazard bags (100 pcs/roll)	<input type="checkbox"/>
<b>Urine</b>	
Urine collection containers	<input type="checkbox"/>
<b>Stool</b>	
Stool containers	<input type="checkbox"/>
Rectal swab	<input type="checkbox"/>
Cary-Blair transport medium	<input type="checkbox"/>
<b>Plague (if suspected)</b>	
Gram stain kit	<input type="checkbox"/>
Rapid diagnostic test (Dipstix AgF1)	<input type="checkbox"/>
<b>Miscellaneous</b>	
Biohazard bags	<input type="checkbox"/>
Racks for handling of specimen tubes	<input type="checkbox"/>
Sterile containers	<input type="checkbox"/>
<b>For packaging and transport of specimens</b>	
Bio-packaging, 1.5 L with ice pack	<input type="checkbox"/>
Cotton wool for cushioning specimen(s) to avoid breakage	<input type="checkbox"/>
Ziploc bags	<input type="checkbox"/>
Address labels for transport of specimens to laboratory	<input type="checkbox"/>
Labels for marking "store in refrigerator" or at 4 °C on outside of shipping box	<input type="checkbox"/>
Case investigation forms and line lists to act as specimen transmittal form	<input type="checkbox"/>
Marking pen (water and alcohol resistant) to label specimen (name, ID number etc.)	<input type="checkbox"/>
Adhesive tape	<input type="checkbox"/>
<b>PPE</b>	
Hand wash (alcoholic, antiseptic and skin protective)	<input type="checkbox"/>
Goggles (reusable) or face shield and anti-fog spray	<input type="checkbox"/>
Face mask N95/FFP2 (cup and folded model)	<input type="checkbox"/>
Overall, complete with head cover (Cat. III CE0120, resistant to penetration by liquid, particle tight, limited splash tight)	<input type="checkbox"/>
Boots or boot covers (disposable)	<input type="checkbox"/>
Examination gloves (non-sterile)	<input type="checkbox"/>

Source: Adapted from Annex 4B (30).

## Annex 6C Checklist for general items to be considered for a field investigation

Equipment and supplies	
Batteries	<input type="checkbox"/>
Body bags	<input type="checkbox"/>
Buckets	<input type="checkbox"/>
Camping kits	<input type="checkbox"/>
Candles	<input type="checkbox"/>
Computer	<input type="checkbox"/>
Camera	<input type="checkbox"/>
Sterile containers (lab)	<input type="checkbox"/>
Cookware	<input type="checkbox"/>
Diesel	<input type="checkbox"/>
First-aid kit	<input type="checkbox"/>
Headlamp/flashlight	<input type="checkbox"/>
GPS	<input type="checkbox"/>
Kerosene lamp	<input type="checkbox"/>
Maps	<input type="checkbox"/>
Mosquito nets	<input type="checkbox"/>
PEP kit	<input type="checkbox"/>
Phones	<input type="checkbox"/>
Plastic sheets	<input type="checkbox"/>
Pharmaceutical items (if drugs and/or vaccines are to be included, please refer to Annex 5A in IDSR 2010 for details)	<input type="checkbox"/>
Power generator	<input type="checkbox"/>
Radio	<input type="checkbox"/>
Stationery (pens, stapler, scissors, clipboard, etc.)	<input type="checkbox"/>
PPE supplies (see Annex 6A)	<input type="checkbox"/>
Laboratory supplies (see Annex 6B)	<input type="checkbox"/>

Source: Adapted from Annex 5A (30).

**Annex 6D. Outbreak investigation forms**

**Annex 6D.1 Case Investigation Form**

Respiratory Infection of Unknown Origin Case Investigation Form			
Date form completed: _____			
Case ID number: _____		Date of symptom onset: _____	
PATIENT INFORMATION			
Family name: _____		Given name(s) _____	
Date of birth: _____		Age: Years _____ Months _____	
Gender <input type="checkbox"/> Male <input type="checkbox"/> Female		If female: <input type="checkbox"/> Pregnant: _____ trimester	
Address: _____			
Contact telephone number(s): _____			
Person completing form if NOT the patient			
<input type="checkbox"/> Relative      Indicate relationship to the patient _____ <input type="checkbox"/> Acquaintance <input type="checkbox"/> Other			
PATIENT ILLNESS			
Date of symptom onset: _____ (dd/mm/yyyy):		Date of hospitalization: _____ (dd/mm/yyyy)	
Symptoms (within the past 10 days)			
<input type="checkbox"/> Fever (____ °C) Temp if known	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Vomiting	<input type="checkbox"/> Yes <input type="checkbox"/> No
Chills	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Diarrhoea	<input type="checkbox"/> Yes <input type="checkbox"/> No
Cough	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Headache	<input type="checkbox"/> Yes <input type="checkbox"/> No
Sore throat	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Seizures	<input type="checkbox"/> Yes <input type="checkbox"/> No
Runny nose	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Rash	<input type="checkbox"/> Yes <input type="checkbox"/> No
Shortness of breath	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Eye infection	<input type="checkbox"/> Yes <input type="checkbox"/> No
Muscle aches	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Other _____	
Complications present at initial presentation			
	Yes	No	Date first recognized (dd/mm/yyyy)
Pneumonia	<input type="checkbox"/>	<input type="checkbox"/>	
ARDS (acute respiratory distress syndrome)	<input type="checkbox"/>	<input type="checkbox"/>	
Acute renal failure	<input type="checkbox"/>	<input type="checkbox"/>	
Cardiac failure	<input type="checkbox"/>	<input type="checkbox"/>	
Consumptive coagulopathy	<input type="checkbox"/>	<input type="checkbox"/>	
Other			
Is the patient a close contact of a confirmed case(s) (if known)			<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
Was the patient admitted to the ICU? <input type="checkbox"/> No ICU in hospital			<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
Did the patient require mechanical ventilation during this hospitalization?			<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
Patient outcome:			<input type="checkbox"/> Discharged alive <input type="checkbox"/> Died <input type="checkbox"/> Unknown
If deceased, specimens collected:			<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
REPORTING INFORMATION			
Name of reporting doctor: _____		Telephone number(s): _____	
Name of person completing form: _____		Signature: _____	
VACCINES AND ANTIVIRALS			

Exposure to influenza antiviral drugs during the last 14 days?  None  
 Yes, patient  
 Yes, household contact  
 Unknown

If yes, name of antiviral:

Vaccination for influenza in current season?  Yes  No  Unknown date:

**OCCUPATION**

- Healthcare worker      If yes, indicate the healthcare facility:
- Laboratory worker      If yes, indicate the laboratory:
- Veterinary worker      If yes, indicate animal contact(s):\*
- Wildlife worker      If yes, indicate wildlife contact(s):\*
- Farm worker (animals)      If yes, specify type of animal(s):\*
- Other, specify: \_\_\_\_\_

\* Indicate contacts for the **10 days before symptom onset**.

**EXPOSURE HISTORY**

**HUMAN**

**In the 10 days prior to the onset of symptoms did the patient:**

Have close contact (within 1 metre) with a person (eg: speaking with, caring for, touching) with a fever and cough or respiratory illness or that died of a respiratory illness?  Yes  No  Unknown

If yes, did the patient have contact with this person's bodily fluids, such as urine, blood, sputum or faeces? Describe the contact

Stay in the same household with anyone who died following the visit?  Yes  No  Unknown

Admitted to hospital?  Yes  No  Unknown

Visit an outpatient treatment facility?  Yes  No  Unknown

If yes, describe what, when and where:

Visit a traditional healer?  Yes  No  Unknown

**TRAVEL**

List all the places to which the patient has travelled outside his/her district/first administrative level during the **last 10 days before** the onset of symptoms:

Location (local, national and international) town/province/state/country	Date of departure	Date of return	Purpose	Mode of travel
--	-------------------	----------------	---------	----------------

Did the patient attend any festivals or mass gatherings in the **10 days before** the onset of symptoms

Yes  No  Unknown      If yes, describe what, when and where

**ANIMAL**

The following questions address exposure to animals in the past 10 days prior to the onset of symptoms

Did the patient visit an agricultural exhibition, farm, zoo or other place where live animals are kept, excluding households in the **10 days before** the onset of symptoms?

Yes  No  Unknown      If yes, describe location, date and direct contact the patient may have had with these animals:

Did the patient have close contact with domestic (including household pets), agricultural or wild animals in his/her home, village, neighbourhood or workplace?

Yes  No  Unknown      If yes, indicate animal, type of contact and location

<input type="checkbox"/> Yes <input type="checkbox"/> No	dogs	<input type="checkbox"/> Yes <input type="checkbox"/> No	pigs
<input type="checkbox"/> Yes <input type="checkbox"/> No	cats	<input type="checkbox"/> Yes <input type="checkbox"/> No	chickens
<input type="checkbox"/> Yes <input type="checkbox"/> No	rodents	<input type="checkbox"/> Yes <input type="checkbox"/> No	wild birds
<input type="checkbox"/> Yes <input type="checkbox"/> No	bats	<input type="checkbox"/> Yes <input type="checkbox"/> No	other
<input type="checkbox"/> Yes <input type="checkbox"/> No	camels		

Were any of these animals sick or dead, in particular poultry or pigs?       Yes  No  Unknown

If yes, indicate type of animal that was sick/dead, type of contact and location

Was the patient aware of any other animals/excreta that are not usually present inside or outside the patient's household (e.g. bats, rodents, stray cats/dogs, foxes, reptiles, etc.)       Yes  No  Unknown

If yes, specify animal:

Did the patient touch (handle, slaughter, butcher or prepare for consumption) animals (including poultry, wild birds or swine) or their remains in the **last 10 days before** the onset of symptoms?

If yes, specify animal, location/source of animal and contact.       Yes  No  Unknown

Did the patient visit a market selling live animals in the **10 days before** onset of symptoms?       Yes  No  Unknown

**FOOD**

Did the patient consume any of the following food or animal derived medicinal items:

Unprocessed or raw vegetables or fruits that may have been contaminated with animal faeces?       Yes  No  Unknown

If yes, specify which and the source.

Uncooked meat (any animal), eggs or uncooked blood products?       Yes  No  Unknown

If yes, specify details, including which animal(s) and the source.

Traditional medicines or home remedies?       Yes  No  Unknown

If yes, specify details including whether an animal or plant product) and its source.

**LABORATORY INVESTIGATION (for each specimen type tested complete a separate page)**

**Date of specimen collection:**

**Type of specimen collected:**

- |   |  |
|---|--|
| <input type="checkbox"/> Nasal swab                     | <input type="checkbox"/> Endotracheal aspirate |
| <input type="checkbox"/> Throat/oropharyngeal swab (OP) | <input type="checkbox"/> Sputum                |
| <input type="checkbox"/> Nasopharyngeal swab (NP)       |  |
| <input type="checkbox"/> Nasopharyngeal aspirate        | <input type="checkbox"/> Blood/serum           |
| <input type="checkbox"/> Tracheal aspirate              | <input type="checkbox"/> Urine                 |
| <input type="checkbox"/> Bronchoalveolar lavage         | <input type="checkbox"/> Faeces                |
| <input type="checkbox"/> Other _____                    |  |

**LABORATORY TESTING**

**Influenza testing**

	RT-PCR Yes or No	Direct or indirect immunofluorescent antibody (DFA or IDFA)	Viral culture	Rapid antigen test
<b>Influenza A</b>	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested
<b>H1</b>	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	
<b>H3</b>	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	
<b>H5</b>	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	
<b>H7</b>	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	
<b>Influenza B</b>	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested	<input type="checkbox"/> Negative <input type="checkbox"/> Positive <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not tested

**Non-influenza testing**

Pathogen	Pos	Neg	Not tested	Pathogen	Pos	Neg	Not tested
RSV				<i>Chlamydia pneumonia</i>			
Human metapneumovirus				<i>Mycoplasma pneumonia</i>			
Parainfluenzavirus (1,2,3)				<i>Legionella pneumonia</i>			
Adenovirus				<i>Streptococcus pneumonia</i>			
Rhinovirus							
Enterovirus				Other			
Coronavirus							
Coronavirus – SARS-CoV							
Coronavirus – MERS-CoV							

**Indicate diagnostic testing method used i.e. PCR, DFA, IDFA, virus culture (cell type)**

**Annex 6D.2 Patient line list template**

Case ID <sup>a</sup>	Case initials	Age	Sex M/F/ unknown	Symptom onset date dd/mm/yy	Current status outpatient/inpatient/ inpatient ICU/ discharged/died	Location hospital/city/ town/village	Case category probable/suspected /confirmed	Epi links	Underlying conditions <sup>b</sup>	Chest X-ray <sup>c</sup>	Specimens collected <sup>d</sup>	Test requested <sup>e</sup>	Test result

- <sup>a</sup> Each case should have a unique ID that is recoded on epidemiological and laboratory forms
- <sup>b</sup> Indicate any underlying conditions e.g. significant immunodeficiencies, medications or other conditions that may alter the patient’s susceptibility or disease course.
- <sup>c</sup> Was a chest X-ray taken? If so, what were the results?
- <sup>d</sup> Examples of specimens: nasopharyngeal (NP) swab, nasopharyngeal wash/aspirate, oropharyngeal (OP) swab, sputum, tracheal aspirate, bronchoalveolar lavage (BAL), pleural fluid, tissue, blood, serum, urine
- <sup>e</sup> Indicate diagnostic test requested: culture, antigen detection, antibody/serology, polymerase chain reaction (PCR), immunohistochemistry (ICH), immunofluorescence (IFA) etc.

Source: Adapted from CDC. *Tools for epidemiological investigation of outbreaks.*



### Annex 6D.3 Contact tracing form

CONTACTS* LISTING FORM													
Contacts listing form filled in by:													
CASE DETAILS													
Case name:						Case ID if assigned:							
Case neighbourhood/village:						Chief or community leader:							
District/town:						Province/region:							
Hospitalized	Y/N	Found in community	Y/N	If hospitalized, hospital name						Date of admission:			
LIST DETAILS OF CASES' CONTACTS BELOW													
Family name	Given name	Relationship to case	Age (yrs)	Sex (M/F)	Head of case's household Y or N	Village/ neighbourhood	Chief or community leader	District/ town	Type of contact <sup>#</sup>	Date of last contact	Last date for follow-up	Date of 1 <sup>st</sup> follow-up	Outcome

\*Contacts are defined as

- Sleeping in the same household with a suspected case or a case
- Direct physical contact with the case (dead or alive)
- Has touched his/her linens or bodily fluids
- Has eaten or touched same sick or dead animal as case

<sup>#</sup> Household, healthcare facility, work, neighbour, other

**Annex 6D.4 Contact follow-up form**

Contact Follow-up Form												
Form completed by												
Name:												
Address:												
CN	Family name	Given name	Age	Sex	Date of last contact	Days of follow-up*						
						1	2	3	4	5	6	7

\* Days of follow-up will depend on the infection and can be extended as needed to any number of days.  
 Mark "0" if the contact has not developed disease symptoms.  
 Mark "X" if the contact has developed symptoms or has died.  
 CN contact number

Annex 6D.5 Laboratory results line list

Laboratory results line listing

Laboratory name:																	
Number of specimens tested:										Epidemiological week:							
Case ID	Specimen type	Date tested	Viral agents*									Bacterial agents*					
			Influenza		RSV	Coronavirus			Adenovirus	Parainfluenza virus	Other	TB	Diphtheria <sup>#</sup>	Whooping cough <sup>^</sup>	Scarlet fever	<i>Haemophilus influenzae</i>	Other
			A	B		SARS	MERS	Other									

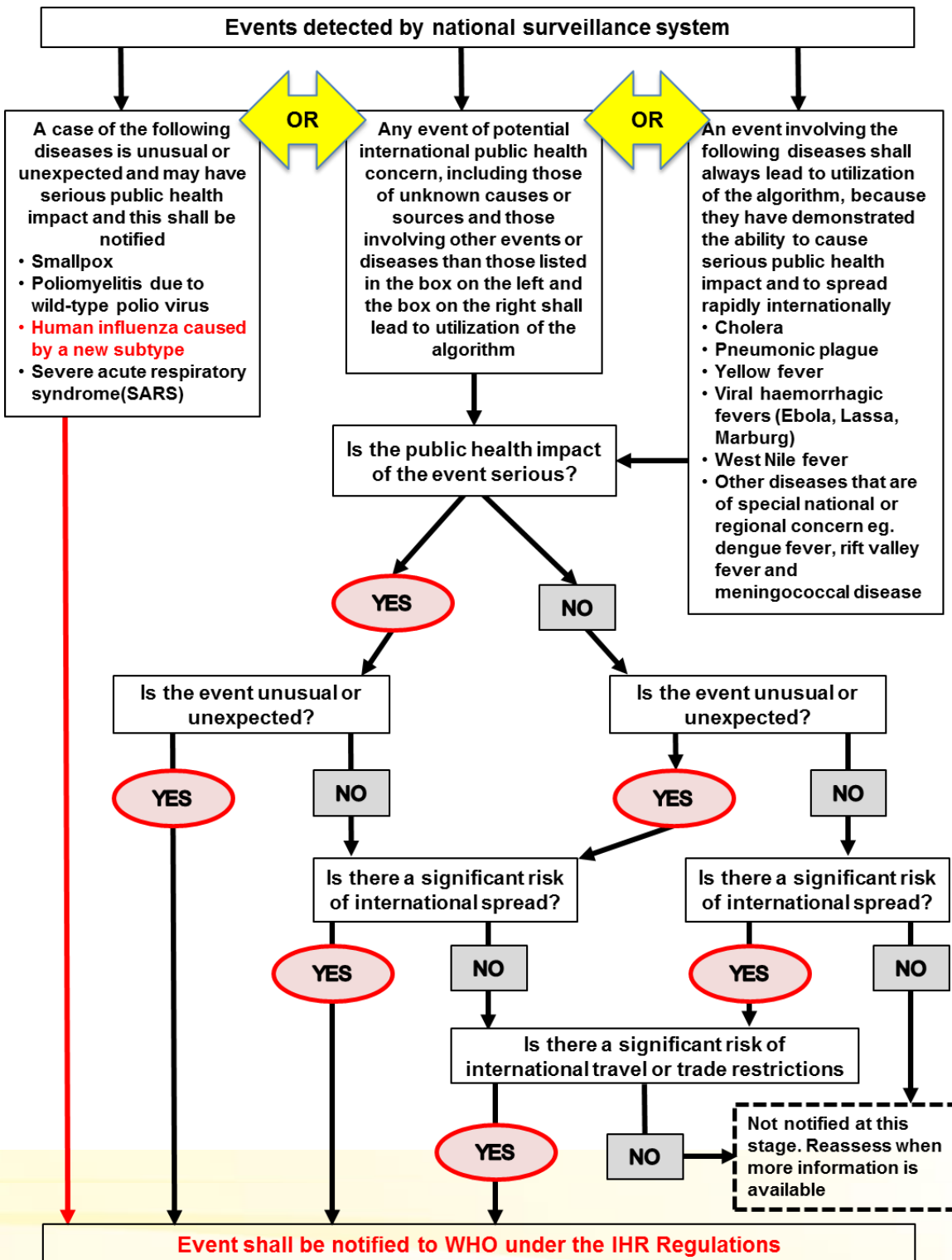
\* If the organism identified is not listed, please list the organism in "Other" column

<sup>#</sup> *Corynebacterium diphtheriae*

<sup>^</sup> *Bordetella pertussis*

Annex 7. IHR Documentation

Annex 7A. IHR decision instrument



## Annex 7B. Example of how to implement IHR instrument

Below is an example of how to apply the IHR decision instrument to an infectious disease with aerosol/droplet transmission. This example is from “WHO guidance for the use of Annex 2 of the International Health Regulations (2005), Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern,” 2010.  
[http://www.who.int/ihr/publications/annex\\_2\\_guidance/en/](http://www.who.int/ihr/publications/annex_2_guidance/en/)

### Case scenario 10: Measles at an international athletics competition

*The MoH in Country N was notified of one confirmed and eighteen suspected measles cases among participants in international athletics competition. The primary case was an athlete from Country P who developed fever and coryza one day before the opening ceremony, Severe conjunctivitis and cough followed, then the onset of a rash. Transmission must have occurred during extensive mingling of athletes from Country P in the prodromal stage before the competition and at several occasions in the domed stadium during the event. Seven suspected secondary cases had their only potential exposure at the opening ceremonies. Three cases with prodromal measles symptoms were unrelated spectators sitting in the same section of the upper deck, more than 30m above the athlete’s entrance. Among those potentially at risk for measles were approximately 600 athletes; 500 coaches and managers from 68 countries; an estimated 2500 volunteers and staff; international media; and approximately 80,000 spectators from numerous countries attending the competition. In essence, the outbreak investigation team identified numerous groups with probable measles exposure.*

*All cases with the clinical picture of acute measles infection have measles IgM antibody in their acute serum specimens (greater than or equal to 1:40 by indirect fluorescent antibody (IFA) test). Nine cases have documented histories of measles vaccination between 9 and 12 months of age. Following onset of the rash, all patients were isolated in their hotel rooms. As live-virus measles vaccine could not have been administered within 72 hours of the most intensive exposure, the local health authorities recommended the use of immunoglobulin for contacts with high risks of complications. Quarantine or closing of this event was not feasible and, because exposure had already occurred, may not have limited secondary spread. Last year, a total of 546 confirmed measles cases and 92% vaccination coverage among children were reported in Country N.*

**Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. Using the decision instrument, please answer the following questions:**

#### **Is the public health impact of this event serious?**

**YES**

Factors indicating that a serious public impact of the event is likely:

- This event may represent a significant public health risk because of: the large-scale exposure to potentially susceptible persons gathered in a confined environment; the extreme infectiousness of the measles virus; the potential to generate serious measles illness; and the difficulty in obtaining timely evidence of measles vaccination from throughout the world.
- Though the high measles vaccination rate in Country N makes it unlikely that this event may cause high morbidity and/or mortality among its population, the event is potentially serious for other states whose residents return from the international competition.

**Is the event unusual or unexpected?**

**NO**

Factors indicating that the event is neither unusual nor unexpected:

- The event is caused by a known agent from a likely common source.
- Evolution of cases is not more severe than expected and the occurrence of the event itself is not unusual for the area.

**Is there a significant risk of international spread?**

**YES**

Factors indicating that international spread is likely:

- There is a high risk for cross-border movement of measles through incubating participants returning to their home country, which endangers the elimination of measles in those countries that already achieved this goal or are on the brink of it.

**Is there a significant risk of international trade or travel restrictions?**

**NO**

Factors indicating that the adoption of trade or travel restrictions are rather unlikely:

- Though the measles outbreak has occurred in association with an international gathering, similar events in the past have not resulted in international restriction on trade and/or travel.

**Based on the above information, this measles outbreak meets two or more of the four criteria of the algorithm in Annex 2 and, thus needs to be notified under Article 6 of the IHR (2005).**

**Learning points:**

1. Disease outbreaks at international events are potentially serious because of the risk of transmission to susceptible persons in large groups gathered in a confined environment.
2. An outbreak of a disease in conjunction with an international gathering may have a high public health impact as a result of exportation of the agent, vehicle or host to countries that have no or almost no indigenous transmission.
3. The public health risk of the occurrence of an infectious agent associated with international gatherings must be considered even in areas without recent activity of that pathogen.
4. Following a joint risk assessment, WHO might facilitate international contact tracing.

## Annex 8. Outbreak communication templates

### Annex 8A Outbreak investigation team Sitrep components

#### Situation report – (event/response name)

**Sitrep no.:**

**Date of issue:**

**Time period of sitrep** (optional if not issued daily or similar):

**Location:**

**Contact details** (phone, fax, email):

#### 1. Investigation team composition

- List members of the investigation team and their area of expertise
- Detail whom the team reports to and whom they get support from

#### 2. Summary of situation to date (what has happened)

- Provide details on surveillance, epidemiology, laboratory results etc.
- Summary can be framed as date, place, time, and who?
- May include a line list of cases identified/epi curves, sites visited, spot maps etc.
- Summary should contain factual information about the outbreak situation

#### 3. Actions to date (what has been done)

- Brief report of actions completed, typically for the period covered by the sitrep
- This may include items such as a review of procedures, briefings, training, site visits, data analysis and information management activities, etc.

#### 4. Actions to be completed (planned activities)

- Brief report of scheduled/planned actions – typically for the period covered by the sitrep
- May include reviews of procedures, implementation of training, site visits, briefings of relevant parties, etc.
- Tables may be used for repeat actions
- Status of actions expect to be by the next sitrep

#### 5. Identification of arising or anticipated issue(s)

- Present a brief description of the issue(s) that are known/reasonably expected to arise before the next sitrep is issued, e.g. shortage of a given resource
- Acknowledgement of significant achievements, failures, etc. can be given here.

**Completed by** (name/role):

**Approved by** (name/role):


**Date:**

**Abbreviations:**

**Notes:**

- Information in the sitrep should be factual and largely without interpretation or conjecture.
- The information/data in the sitrep should cover the period between the last and the next sitrep.
- Sitreps should be brief, i.e. able to be read in 3–5 min. More detailed information can be contained in a report.
- Sitreps should be specific to a given functional area, i.e. do not present data outside the terms of reference.
- Ensure inclusion of important information: sitrep number, event/response title, sitrep date and time period covered, location and contact details.





# World Health Organization

Change the WHO logo according to your region. All WHO logos in different languages are available on the HQ intranet.

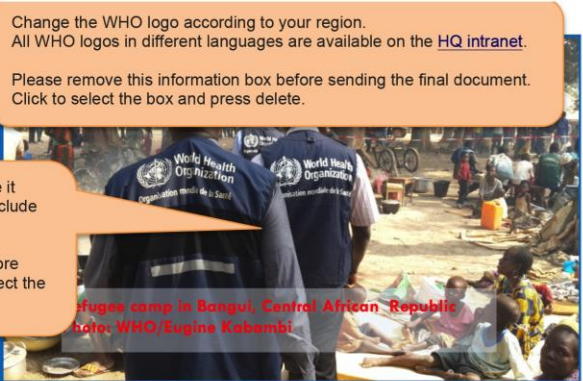
Please remove this information box before sending the final document. Click to select the box and press delete.

Situation report #  
**DD-MMM-YYY**


Name of the Country  
Emergency type e.g. floods, earthquake, conflict

Remove the example photo and replace it with your photo or a map of the area. Include caption and photo credit.

Please remove this information box before sending the final document. Click to select the box and press delete.




Refugee camp in Bangui, Central African Republic  
Photo: WHO/Eugene Kabambi




### ##

**AFFECTED**




### ##

**DISPLACED**




### ##

**REFUGEES**



### ##

**INJURED**



### ##

**DEATHS**

WHO	HIGHLIGHTS
# ### STAFF IN THE COUNTRY	<ul style="list-style-type: none"> <li style="color: red; margin-bottom: 10px;">• Type in max four key messages drawn from the report below</li> </ul>
MEDICINES DELIVERED TO HEALTH FACILITIES/PARTNERS*	
# ### ANTIBIOTICS	
# ### CHRONIC DISEASE MEDICINES	
# ### ANTI-DIARRHOEA MEDICINES FOR CHILDREN	
FUNDING US\$	
# ### % FUNDED	
# ### REQUESTED	
<b>HEALTH SECTOR</b>	
# ### HEALTH CLUSTER PARTNERS	
# ### TARGETED POPULATION	
MEDICINES DELIVERED TO HEALTH FACILITIES/PARTNERS*	
# ### ANTIBIOTICS	
# ### MEDICINES FOR CHRONIC DISEASES	
# ### ANTI-DIARRHOEA MEDICINES FOR CHILDREN	
<b>HEALTH FACILITIES</b>	
# ### TOTAL NUMBER OF HOSPITALS	
# ### HOSPITALS FUNCTIONING	
<b>HEALTH ACTION</b>	
# ### CONSULTATIONS**	
# ### SURGERIES	
# ### ASSISTED DELIVERIES**	
# ### REFERRALS	
<b>VACCINATION AGAINST</b>	
# ### POLIO**	
# ### MEASLES**	
<b>EWARN</b>	
# ### SENTINEL SITES	
<b>FUNDING US\$</b>	
# ### % FUNDED	
# ### REQUESTED	

\*coverage for one month

\*\*if denominator available give rate



Situation update

Type any update on the disaster/crisis, include information on the affected area and affected population (e.g. number of affected, known vulnerable groups, including ethnic minorities, reports of population movements.

Public health concerns

Type description and analysis of the current or generic public health concerns, including morbidity data, such as number of cases, incidence or proportional morbidity of prominent communicable and non-communicable diseases and interpretation.

Health needs, priorities and gaps

Type the current needs and remaining gaps, including functionality of health facilities and availability of health services, health staff, essential drugs, vaccines and supplies. Use the HeRAMS checklist (i.e. Health Response Domains) as a reference for the main headings. Use SPHERE as reference for benchmarks.

WHO action

Describe WHO surge staffing and the main WHO activities, in the different domains (ie. coordination, epidemiological surveillance, vaccination, reproductive health, mental health, WATSAN, nutrition, medical and drug supplies, etc.)

This should be extracted from the health cluster bulletin.

Resource mobilization

Describe the resource mobilization achievements and gaps.

FUNDING STATUS OF APPEALS US\$				
	NAME OF THE APPEAL	REQUIRED FUNDS	FUNDED	% FUNDED
WHO	Type the name	Type the amount in US\$	Type the amount in US\$	Type the%
HEALTH SECTOR	Type the name	Type the amount in US\$	Type the amount in US\$	Type the%

Background of the crises

Type any background information on crisis.

Nature and scale of disaster: intensity, geographic region affected, including area in square kilometres and type of terrain, accessibility, weather conditions, presence of aftershocks.

Presence of other hazards: e.g. conflict, after shocks.

Background socio-economic and political information for the country and affected regions: Socio-economic indicators (e.g. per capita income, political stability, main sources of livelihood).

Background on health

Remove all the instructions before typing in text.

Please remove this information box before sending the final document. Click to select the box and press delete.

### Contacts:

Name, email: , telephone:

## Annex 9. Sample outline of an outbreak investigation report

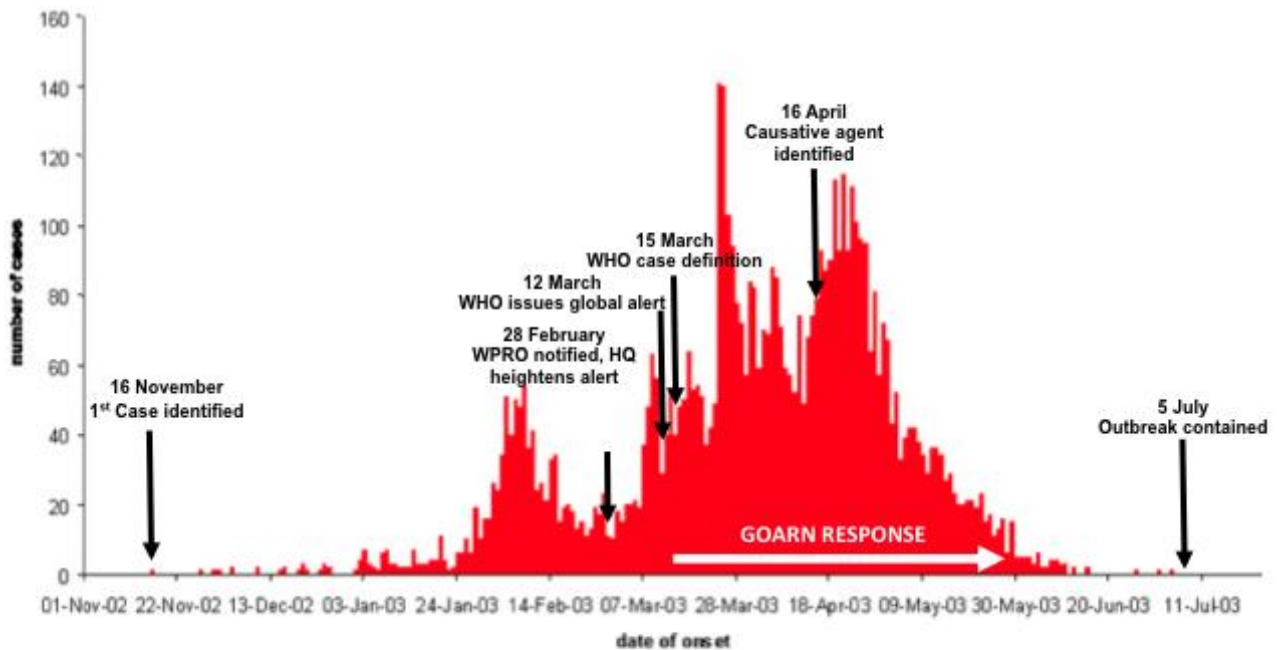
Title/description (include disease/condition investigated)	
Period	Place (Villages, neighbourhoods, district, province)
<b>Executive summary</b>	
<b>Introduction</b>	
Background	
Reasons for investigation (public health significance, threshold met, etc.)	
Investigation and outbreak preparedness	
<b>Methods</b>	
Dates of investigation	
Site(s) of investigation (healthcare facilities, villages, other)	
Case-finding (indicate what was done regarding case-finding, e.g. register review, contact investigation, alerting other health facilities, other)	
Laboratory specimen collection	
Description of response and intervention (include dates)	
Data management	
<b>Results</b>	
Date and location of first known (index) case	
Date and health facility where first case was seen by the healthcare system	
Results of additional case-finding	
Laboratory analysis and results	
With text, describe key features of results of time, place and person analysis	
Detailed results by time (epi curve), place (map), and person characteristics (tables) and line lists	
Results of response and evidence of impact	
<b>Interpretations, discussion and conclusions:</b>	
<b>Recommended public health actions</b>	
Comment on the following levels: community, health facility, district, partners, provincial and national.	
<b>District epidemic committee chairperson</b>	
Name	Signature
<b>District medical officer</b>	
Name	Signature
Date report completed:	

Source: Adapted from Annex 7A (30).

## Annex 10. Chronology of an outbreak

### Epidemic curves - Severe Acute Respiratory Syndrome (SARS)

**Probable cases of SARS by week of onset  
Worldwide\* (n=5,910), 1 November 2002 - 10 July 2003**



\* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

<http://www.who.int/csr/sars/epicurve/epiindex/en/index1.html>

### Time line of influenza A[H1N1]pdm09 pandemic by epidemiological week 2009-2010

